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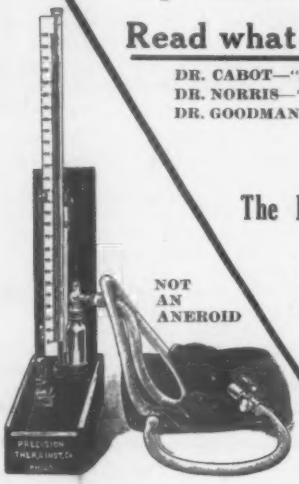

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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

JUNE, 1916

ORIGINAL ARTICLES

THE RESPIRATION CALORIMETER IN CLINICAL MEDICINE.*

By Eugene F. DuBois, M.D.,
NEW YORK CITY.

(From the Russell Sage Institute of Pathology in affiliation with the Second Medical Division, Bellevue Hospital, New York.)

In these days when the housewives speak in terms of calories and the newspapers deal with vitamines it may be well for clinicians to examine once more the fundamental principles of nutrition. Patients no longer demand medicines but they do expect diets, and if they are at all up with the magazine literature, they are better informed on the subject than the text-books which most of us studied in the medical schools. The diets which patients receive in most of our hospitals were laboriously compiled several generations ago and modified from time to time by hospital dietitians. Foods were classified according to their solidity as administered, regardless of what happened in the stomach. Details were left to the head nurse and sometimes to their probationer, and while the patient always had the veto power because he could vomit he was seldom able to initiate legislation.

The science of nutrition in disease must be founded upon experiments in calorimetry and the respiratory metabolism. It may be well at this point to state just what is meant by the term metabolism. The word in itself indicates the transformation of matter and refers to the breaking down of foods, to their absorption, and to the building up of body tissues. The term also refers to the

* Lecture delivered before the Harvey Society of New York, November 27, 1915.

oxidation of food-stuffs and of body tissues, with the consequent liberation of warmth and energy. Analysis of food, urine and blood gives an incomplete picture, and it is only through a study of the gaseous exchanges in the tissues that we can study the total metabolism. There are many phrases which have the same meaning as total metabolism. Frequently it is spoken of as *the* metabolism. Sometimes it is called the total energy requirement, total food requirement or heat production, total oxidative processes or total gaseous exchange.

In the years between 1892 and 1908 there was no work being done on this subject in our American hospitals, although Atwater and his successor Benedict, in Middletown were making classical experiments on normal men, and Lusk, here in New York, was making similar experiments on dogs. During this same period in Germany the respiratory metabolism was being studied in a dozen clinics and the investigators were hoping that at some time means would be found to apply the apparatus of Atwater and Benedict to the study of disease, since this alone would solve certain problems. About seven years ago, Benedict and Joslin,[1 2 3] in Boston, began to study the respiratory metabolism of diabetes, and four years ago investigation of the gaseous exchanges of typhoid patients was begun in Bellevue Hospital.[4] Shortly afterward the directors of the Russell Sage Institute of Pathology decided to turn over their funds to Professor Graham Lusk for a period of five years in order that a calorimeter might be built and maintained in Bellevue.

This respiration apparatus is perhaps the most complicated piece of machinery used in modern medicine, but the principles involved in its construction are simple. The description would seem to be a mass of technical details were it not for the fact that it illustrates beautifully the manner in which medicine is founded on physiology and physiology on physics and chemistry.

The first Atwater-Rosa[5] calorimeter in Middletown was a large chamber in which a man could lie in bed, stand up or ride a stationary bicycle. This apparatus is now in Washington, under the charge of Langworthy and Milner[6] who have made many improvements. Atwater's work, however, has been chiefly continued by Dr. F. G. Benedict,[7 8] of the Nutrition Laboratory in Boston, where great advances in the science of calorimetry have been made. Dr. H. B. Williams,[9] of New York, who constructed the small and very accurate calorimeter for Lusk at the Cornell Medical College, has added many ingenious devices. The Sage calorimeter was finished by Mr. J. A. Riche and Mr. G. F. Soderstrom,[10] in the early part of 1913. It has all the modern improvements and is especially adapted for clinical work where observations must be short. Fortunately it is situated in a room near the medical wards of the second division of Bellevue. It is next door to a small diet kitchen

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and metabolism ward, where three specially trained nurses weigh out the food and collect the specimens.

The calorimeter itself consists of a copper box about the size of the lower berth of a sleeping car. It contains a comfortable bed and is provided with two windows, a shelf, a telephone, a fan, a light, and a Bowles stethoscope for counting the pulse. The ordinary experiment takes about as long as a trip from New York to New London, and there is an agreeable absence of cinders. Patients, as a rule, doze from time to time or else try to work out some scheme by which they can amuse themselves without moving. After three or four hours they are rather bored by the quiet, and the observations are not prolonged beyond this time. They are allowed to turn over in bed once or twice an hour, but reading and telephoning are discouraged, since these increase the metabolism. The air in the box is fresh and pure, the patient suffers no discomfort, and objections to the procedure are very infrequent. Most of the patients are only too glad of the extra attention, and they insist that the calorimeter has a marked therapeutic value.

The apparatus has two distinct functions: (1) the physical measurement of the heat production of an individual by the method of direct calorimetry; (2) the chemical measurement of his gaseous exchanges and the calculation of the heat by the method of indirect calorimetry. Both depend on the fact that the apparatus is a closed circuit, absolutely shut off from the surrounding atmosphere in such a manner that everything eliminated by the subject is caught and measured.

None of the heat radiated from the man's body can travel through the insulating walls of the calorimeter. All is caught and measured in a stream of cold water flowing through a pipe in the top of the box. It is necessary to measure also the heat dissipated from the body in the vaporization of moisture from skin and lungs. A man loses about one-quarter of the total heat in this manner, and the 20 to 30 grams of water evaporated each hour are caught in a sulphuric acid bottle in the ventilating current. The grams of water multiplied by the factor for the latent heat of vaporization gives us the calories so eliminated. These measurements are very accurate, but it is difficult to determine how much heat a man stores in his body when his temperature rises or how much he releases from his body when his tempertaure falls. The rectal thermometer does not always tell us of the changes in the average body temperature, and an error of 0.1° C. may cause an error of 5 or 6 calories. It is for this reason that direct calorimetry is difficult when the fluctuations of temperature are great. When short periods are employed we therefore place our chief reliance on the method of indirect calorimetry.

This second method is entirely chemical; and, since it involves

a different set of measurements, it serves as an excellent check on the accuracy of the results. The calorimeter is air-tight, and is connected with a series of absorbing bottles by means of a closed circuit or pipes. Air is drawn from the foot of the box by a rotary blower, passed through a bottle of strong sulphuric acid to remove the water vapor and then through weighed bottles of soda-lime and sulphuric acid, which catch the carbon dioxide. By noting the change in weights of these bottles the amounts of water and carbon dioxide removed may be determined. The air thus purified is returned to the box and is used again and again. Meanwhile the subject is consuming oxygen, and this would decrease the volume of gases within the box were it not for the fact that oxygen is automatically admitted from a weighed bomb to compensate exactly for the amount consumed. If we divide the liters of carbon dioxide produced by the liters of oxygen consumed we obtain the respiratory quotient. Knowing this and the amount of nitrogen eliminated in the urine it is possible to calculate the grams of protein, fat, and carbohydrate metabolized each hour. From their well-known heat values we can reckon out the calories produced. With the exception of a portion of the protein molecule each food-stuff is oxidized to the same end-products and with the same liberation of heat in the body as in the Liebig combustion furnace or the bomb calorimeter. The process is slower but just as complete, and there is no loss of energy.

The experimental procedure is not very complicated. A patient is given his ordinary supper in the evening. The next morning his breakfast is withheld and he is put in the calorimeter at about ten o'clock. By eleven o'clock the machine is brought into thermal equilibrium and the experiment is started. At the end of each hour the ventilating current is switched to a new set of absorbing bottles, and by one or two o'clock the observation is over. Calculations consume an hour or so more, and as soon as the urinary nitrogen is determined we have the following information in regard to the patient in hourly periods: consumption of oxygen; output of carbon dioxide; output of water and the total calories; percentage of calories furnished by protein, by fat, by carbohydrate; percentage of heat lost by vaporization, by radiation, and conduction and by storage in or loss from the body; and finally, total metabolism and its relation to the average normal figure, this total metabolism being measured by two independent methods. As may be supposed, these activities keep the three observers fairly busy, since they involve about 40 weighings, 500 temperature readings, and the writing of over 4000 figures.

The accuracy of the calorimeter is tested at regular intervals by burning known amounts of alcohol and comparing the actual findings with the theoretical. In 9 such tests the average error

for heat production was 0.9 per cent., for oxygen 1.2 per cent., for carbon dioxide 0.8 per cent. The total errors are even smaller.

It is hardly necessary to point out that the results obtained with the calorimeter are due to the team work of the whole staff, including the nurses who administer the diets and the chemists who analyze food, blood, urine, etc. Those chiefly responsible for the work here presented are: Dr. Lusk, the scientific director; Mr. Gephart, Dr. Meyer, Mr. Soderstrom, Mr. Harries, Miss Magill, all of the Sage staff, and out associates, Dr. Warren Coleman, Dr. F. M. Allen, and Dr. F. W. Peabody.

There have been many types of apparatus used in the study of the respiratory metabolism in disease.[11] Unfortunately time does not permit of their description, but one cannot help mentioning by name the Pettenkofer-Voit chamber, the Zuntz-Geppert apparatus, the Benedict Unit,[12 13] and the Paschutin calorimeter.

The main object of all investigators has been to determine the heat production of the patient while at complete rest fourteen hours or more after the last meal. This is the so-called basal metabolism, and is of interest only when compared with the figures obtained on normal individuals. Since it is impossible to measure the metabolism of many of our patients when they are entirely recovered, it is necessary to calculate what the man's metabolism would be were he normal. Here lies the most difficult problem. Controversies have raged more fiercely about the normal controls than about the pathological cases. It has been said that a man is as old as his arteries. It may also be said that a piece of research work is as good as its normal controls.

The normal controls used by investigators up to the last few years often showed a variation of 50 per cent. above or below the average. It was discouraging to run the calorimeter within an error of 1 or 2 per cent. and then compare the results with such an uncertain figure. Now this variation in the normals was largely due to the manner in which the results were expressed. If we leave the calculations, as was previously done, in the stage of cubic centimeters of carbon dioxide per kilogram of body weight there might be a large apparent variation between two men whose heat production is identical. Part of this error is eliminated if we express the results in calories, and still more eliminated if we base our calculations on surface area rather than body weight. A large man, of course, gives off more heat than a small man, but for each kilogram of body weight the small man has the higher metabolism. Rubner[14] demonstrated many years ago that the metabolism is proportional to the surface area of the body and that for each square meter of skin large men, small men, dogs, horses, and mice have about the same heat production. Just why this should be we do not know. It reminds us at once of Newton's law that the cooling of bodies

is proportional to their surface area, but the metabolism does not follow this law when the external temperature is raised or lowered.

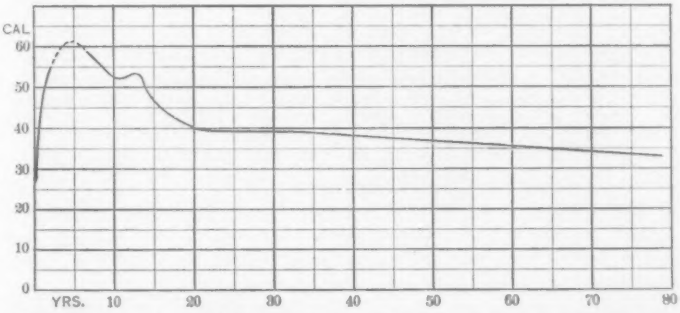
There are several formulas which allow us to calculate the surface area of a man. Meeh's[15] formula, which is proportional to the two-third power of the weight has been the standard for over a generation, and up to the last year entered into almost all the calculations. One divided the calories produced per hour by the square meters of surface area and obtained the calories per square meter per hour. Very recently the accuracy of Meeh's formula was investigated by the Sage staff. Mr. Delafield Du Bois[16] devised a method of measuring the skin area which has been applied to ten individuals of every conceivable shape. He found an average plus error of 16 per cent. in Meeh's formula and an error of 36 per cent. in fat subjects. To correct these the so-called "linear formula" was devised and also a simpler formula based on height and weight.[17]

It is interesting to group the normal controls studied in the Sage calorimeter[13] with the large number of healthy men and women studied by Benedict, Emmes, Roth and Smith in Boston,[19 20 21 22 23] and also by Palmer, Means, and Gamble.[25] If we plot the men under fifty years of age according to calories per square meter of surface area we find that all are within 15 per cent. of the averages and 86 per cent. are within 10 per cent. of the average. According to Meeh's formula thin people have an increased metabolism and fat people a very low metabolism. Using the more accurate linear formula, Means[24 25 26] has found the metabolism in most cases of obesity to be within normal limits, and if we recalculate the figures for groups of thin men and fat men according to their true surface area the results in the two groups are almost identical.

We can therefore feel certain that with men between the ages of twenty and fifty the metabolism of each individual is proportional to his surface area whether he be short or tall, fat or thin. We can compare all our pathological cases with the normal average basal metabolism of 34.7 calories per hour per square meter of surface according to Meeh's formula, or, better still, 39.7 per square meter according to the new so-called linear formula. The normal variation from this average is plus or minus 10 per cent. and a few apparently normal men show a variation of 15 per cent. We cannot consider the metabolism of an individual patient to be abnormal if within these limits, but if a group of patients gives an average of more than 10 per cent. from the normal base line we can feel certain that there is a pathological change in the heat production in that particular disease.

Comparisons of different persons can be made only by determining the basal metabolism. There are many factors which cause certain groups of normal individuals to depart materially from our

mean figure of 39.7 calories per square meter per hour. Women give an average about 6 per cent. below this,[22] athletes are about the same distance above, as has been shown by Benedict and Smith.[21] Age causes a marked difference which will be discussed later. The metabolism seems to be higher in the afternnoon than in the morning, and during profound sleep there is a drop of 5 to 20 per cent. The metabolism is 5 to 10 per cent. higher sitting upright in a chair than when lying down, but it has recently been found that the metabolism of subjects propped up comfortably in a steamer chair is a little lower than when they are lying flat in bed.[27] This throws some light on one of the many causes of the assumption of the orthopneic position by patients. It lends scientific support to the empirical observation that a lazy man is happiest with his chair tilted back and his feet on the desk.



Variation of basal metabolism with age. The curve shows the changes in the level of the heat production from birth to old age. The results are expressed in terms of calories per square meter of body surface per hour. Only male subjects were used in making the curve. The surface area was estimated by the linear formula or the comparable height-weight formula except in the case of the infants, where it was necessary to use Lissauer's formula. The normal variation from the above line is plus or minus 10 per cent. Details of this curve will be published in the Archives of Internal Medicine.

As I have said, the basal metabolism is measured fourteen hours or more after the last meal because food stimulates the metabolism. This is due to the so-called specific dynamic action of foods, and is greatest in the case of protein and least in the case of carbohydrate. The phenomena, first discovered by Rubner,[28] have been studied in great detail by Lusk,[29] using the dog calorimeter at the Cornell Medical College. He has found that the specific dynamic action of protein is due to the stimulus of the metabolism products of amino-acids acting upon cell protoplasm, and that although the preliminary cleavage products of fat and carbohydrate do not appear to be direct stimuli, yet when they are present in excess in the fluid bathing the cells, the heat production is increased. With the normal controls in the Sage calorimeter[18] a standard

protein meal containing 10 grams of nitrogen causes an average increase of 12 per cent. in the five to six hours after its ingestion, and 100 grams of dextrose causes an increase of 9 per cent. These same meals have been used to test the specific dynamic action of foods in typhoid fever and exophthalmic goitre.

The curve showing the effect of age on heat production is of special interest. Magnus-Levy and Falk[30] demonstrated that the metabolism was high in childhood and low in old age, and no one will doubt this who has compared the amounts of food consumed by children and by their grandparents. We have now at our command a large number of observations made at all ages except the period between the second and sixth years. The reason for this gap is apparent. The shortest experimental period is ten minutes, and normal children of this age are never quiet for this length of time. The metabolism of infants has been studied by Howland,[31] Benedict and Talbot,[32 33 34] by Murlin and Hoobler,[35] Bailey and Murlin[36] and others. Eight boy scouts, not long ago, were studied in the Sage calorimeter[37] and made to keep quiet by a system of fines and rewards. If we tabulate these with all the other children and adults we can trace a curve which shows the heat production per square meter of surface at different ages, and compare it with the average adult figure. During the first few weeks of life the metabolism is very low, after which it rises rapidly until at the end of the first year it is 50 per cent. above the adult level. The curve reaches its acme in the almost unexplored period between two and six years and then falls fairly rapidly until the age of twenty years. After this the decrease is extremely gradual.

Just why newborn infants should have such a low metabolism we do not know. It is conceivable that the high metabolism of older children is in part due to the relatively large size of the head, body, and especially the liver. Men with their legs cut off resemble babies in the relative proportions of body and extremities. Two such individuals studied in the calorimeter have been found to have a high metabolism. This would not explain the high metabolism of the boy scouts who have reached the adult proportions although they have not attained adult size. Theorists might go so far as to say that the increased heat production proves in itself an increased thyroid activity in childhood. It is safer for several reasons to ascribe it to some unknown stimulus associated with growth. For the level of metabolism falls as the rate of growth decreases, but rises again in the case of the boy scouts just before the onset of puberty, a period when the rate of growth is once more accelerated. Again, in adult life the nearest approach to the growth of childhood is found in convalescence from acute infectious diseases, and there is a distinct rise in metabolism in the convalescence from typhoid fever.[4 38]

METABOLISM IN DISEASE. The most striking disease from the standpoint of changes in the total metabolism is exophthalmic goitre, and clinicians who pay no attention to the gaseous exchanges neglect the most important phase of this malady. Friedrich Müller first called attention to the high metabolism in Basedow's disease by noting the nitrogen and weight losses of patients taking enough food to maintain normal subjects in nutritive equilibrium. Magnus-Levy [40] [41] found the gaseous exchanges very high in Graves's disease and very low in myxedema.[42] His results have been amply confirmed by Stüve,[43] Hirschlaff,[44] Salomon[45] and others, and by those of us working with the Sage calorimeter.[46] If we group 33 cases of hyperthyroidism studied by other investigators with the 11 studied in New York, we find that the increase in metabolism is strictly proportional to the severity of the clinical symptoms. One fatal case of Hirschlaff's in the last two weeks of life showed an increase of 120 per cent. above the average normal and two severe but non-fatal cases at Bellevue have given results which are 100 per cent. above the normal. In general, it may be said that very severe cases show an increase of 75 per cent. or more, severe cases 50 per cent. or more, moderately severe and mild cases less than 50 per cent., while a few mild, atypical or operated cases may be within normal limits.

This increase in metabolism is the most striking effect of thyroid activity, and it is equalled in no other disease. In cretinism and myxedema the metabolism may be 25 to 50 per cent. below the normal level. Thyroid extract raises the metabolism in these conditions and has a similar though less constant effect on normal men and obesity patients. No other glandular extract yet examined has this property in any significant degree. Many of the symptoms of hyperthyroidism are secondary to the abnormal heat production. The flushed, warm skin and the sweating are physiological methods of dissipating extra heat. The increased appetite and the loss of weight that sometimes occur in spite of this are the results of increased calorific requirements. Part of the tachycardia is certainly due to the greater demands for oxygen.

Most of the investigators who have studied the gaseous exchanges in this disease have used the level of the metabolism as an index of the effect of treatment. This procedure is perfectly logical, and it is particularly desirable to have some purely objective guide to therapeusis in a disease where there is so much psychotherapy on the part of the physician and patient. Previous observers have found no change in the metabolism after the administration of rhadogen,[45] Roentgen rays,[47] and the serum of thyroidectomized animals,[45] but have established a prompt drop after partial thyroidectomy.[48] In the cases observed at Bellevue a fall of 10 or 15 per cent. has resulted from rest alone, and none of the other therapeutic measures tried gave any better results. These included

Beebe's serum, ergotin, and quinin hydrobromate, and finally thyroid residue. But since the two former methods were tried on only one patient it is nor fair to condemn them. With several patients the thyroid arteries were ligated, and it was found that this procedure caused a sharp rise in the metabolism which fell subsequently to its former level. The operative procedure, although very conservatively done under local anesthesia, increases temporarily the activity of the gland. There is as yet no proof that any form of medical treatment or ligation of arteries causes a greater reduction in metabolism than rest in bed. Several important facts have been brought out in regard to the administration of food to Basedow patients. They need large amounts of food with an abundant, though not excessive, protein ration. Von Noorden[49] has warned us against the use of large amounts of protein and especially meat, assuming that it causes a greater rise in heat production in sickness than in health. Pribram and Porges[47] found that after a diet with large amounts of meat the metabolism was slightly increased, but not more so than in normal people. Undeutsch[48] found that the protein of meat causes less stimulation than vegetable proteins. With the Sage calorimeter it has been found that the specific dynamic action of protein and carbohydrate with exophthalmic goitre patients is not appreciably different from the normal, and that there is no significant difference between the effects of meat and the same amount of protein in milk and eggs. It has taken a large amount of work to disprove the hypothesis of a prominent specialist. Still, it is a great relief to know that we need not worry our patients with restrictions on the kinds of proteins they take. The protein ration should contain about 12 to 15 grams of nitrogen a day, which is the amount ordinarily consumed.

The carbohydrates are readily metabolized in spite of the moderate glycosuria found in severe cases. Except in the true cases of diabetes with goitre it is an abnormality of mobilization rather than utilization. One of the severe cases at Bellevue Hospital was able to derive 90 per cent. of his calories from the oxidation of carbohydrates in spite of a marked glycosuria. A severe case of diabetes could not have derived 10 per cent. of his calories from this source, and even a mild case would scarcely have reached the figure of 50 per cent. Goitre patients use up carbohydrates rapidly, and fourteen hours after their last meal are maintaining themselves almost entirely on fat and protein.

In regard to the medical treatment of Graves's disease the calorimeter may be a therapeutic Nihilist, but it is a dietetic enthusiast, and it is also a strong supporter of the belief that mental and physical rest are essential in the treatment of severe cases.

Diabetes Mellitus. The Harvey Society is fortunate in having, almost every year, a lecture devoted exclusively to the fascinating

subject of diabetes mellitus. The respiratory metabolism was discussed last year in a masterly fashion by Joslin,[53] who, with Benedict, in Boston,[1 2 3] has done an enormous amount of work on this subject. During the past year, working in coöperation with Dr. Allen,[51] of the Rockefeller Hospital, it has been possible to study in the greatest detail one particularly severe case of diabetes snatched from coma by the Allen fasting treatment. This case and several others also studied have given such striking confirmation to the views held by Lusk, [52 53 54 55] for many years, that it is impossible to pass the subject by. Lusk was the first to maintain that a patient who was completely diabetic would excrete not only all the ingested carbohydrate but would also turn about half of the protein molecule into sugar and excrete it in the urine. Under these conditions the excess of excreted sugar over ingested would be about three and a half times the nitrogen in the urine: in other words, the D : N ration would be 3.65. Under these circumstances the respiratory quotient would be depressed below that of fat by the incomplete combustion of protein instead of being raised by protein as with normal people. The lowest possible quotient in health is 0.72, and in complete diabetes with the D : N ratio 3.65, Lusk has calculated that the quotient might be depressed to 0.69. One of the severe cases above mentioned with the D : N of 3.5 showed a quotient of 0.697, another with the D : N of 3.1 gave a quotient of 0.692. There was absolutely no evidence of any formation of sugar from fat. The D : N ratio if determined under the proper precautions is certainly the best guide as to the severity of the case.

The effect of the Allen[56] fasting treatment in the severe case most completely studied was to cause a gradual rise in the quotient as the D : N ratio fell and the glycosuria cleared up. After the fast the curious phenomenon mentioned by Joslin[50] was noted. There was a rise in quotient indicating the combustion of carbohydrate from some unknown source. This may be stored glycogen, excess of sugar in blood and tissues, or perhaps it may be due to the oxidation of acetone bodies.

Another effect of the fast was the marked fall in total metabolism. The patient was brought to a condition where his low food requirement could be met by his improved though still damaged metabolic functions. The metabolism was reduced to a point even lower than that reached by normal men fasting a long time.

This brings us to the question of the total metabolism in diabetes, still the subject of controversy. The older investigations by Pettenkofer and Voit,[57] Nehring and Schmoll,[58] Magnus-Levy,[59] Du Bois and Veeder[60] and others indicated only a slight increase in total metabolism. More recently Benedict and Joslin,[1 2 3] who have studied a large number of cases, have maintained that the metabolism averages about 15 per cent. above the normal in severe

diabetes, and Rolly[61] and Leimdörfer[62] reached the same conclusion. Lusk[63] has gone over the results obtained by Benedict and Joslin using different normal controls for the purposes of comparison, and has concluded that the metabolism is but slightly increased. An interesting light has been thrown on this subject by the new method of calculating the surface area. It was noted in one severe case of diabetes, studied before the fast at Bellevue Hospital, that the metabolism was 2 per cent. above the average figure according to Meeh's formula, but 8 per cent. below according to the true surface area. Patients with severe diabetes are usually very thin, and in such cases comparisons based on Meeh's formula are untrustworthy. If we recalculate the severe cases of Benedict and Joslin by means of the new height-weight formula we find that the average is about 3 per cent. above the standard figure of 39.7 calories per square meter per hour. The cases studied at Bellevue were all below the normal, but some of them were low on account of fasting. (One patient very recently studied showed a slight increase in metabolism for a few days. His acidosis and also his nitrogen elimination were unusually high.)

Typhoid Fever. Typhoid lends itself particularly well to a study of the changes in metabolism which occur in fever. It is more uniform in its course than most fevers, is protracted, is often severe, and is with us every autumn. There are several factors at work in a typhoid patient: (1) toxemia, (2) fever, and (3) more or less starvation. Since the introduction of the Shaffer-Coleman[65] high calory diet this last factor has almost disappeared, leaving a much more satisfactory disease for the patient and for the scientific investigator. The work done on the nitrogen metabolism has been voluminous, and the controversy concerning the toxic destruction of protein is still violent. The respiratory metabolism has been studied by many investigators, notably Kraus,[66] Svenson,[67] Grafe,[68] and Rolly.[69] At Bellevue Hospital 134 observations with the small Benedict apparatus have been made by Coleman and the writer and 61 with the Sage calorimeter.

The total metabolism in typhoid fever shows an increase which is roughly proportional to the rise in temperature. At the height of the fever it averages about 40 per cent. above the normal, but in some cases may be more than 50 per cent. above. Patients who are liberally nourished with the high calory diet of Coleman and Shaffer do not have a greater heat production than patients on low diets. The Sage calorimeter has shown that the specific dynamic action of protein and glucose is much smaller than normal, and in fact almost absent in typhoid fever. The practical application of all this is that typhoid patients need more food than normal men under similar conditions, and that food even in large amounts is well absorbed and does not increase the heat production, as was previously feared. Typhoid patients like all others with high

metabolism use up their carbohydrate food and glycogen stores rapidly, and this type of food should be given in large amounts if we do not want the patients to subsist on protein and fat obtained chiefly from their own tissues.

The actual heat production of most of the typhoid patients is between 2000 and 3000 calories a day. Such amounts, as a rule, can be readily administered, and to me personally it hardly seems necessary to give more than 3000 calories a day unless the patient wants it. Dr. Coleman, whose experience is much greater than mine, believes that patients do best on larger amounts, since these alone will prevent the loss of body protein.

A series of careful experiments has been made in which the nitrogen and respiratory metabolism was studied at the same time. Now a normal man can be maintained in nitrogen and weight equilibrium if given a moderate amount of protein and enough calories to cover the heat production as calculated from the basal metabolism, with allowance for food stimulation and muscular activity. It has been possible by means of the Sage calorimeter to determine the actual heat production of a series of typhoid patients. In the adjoining metabolism ward the head nurse, Miss Magill, and her assistants have skilfully administered food in sufficient amount amply to cover the caloric output. Yet the patients have shown distinctly negative nitrogen balances during the febrile period, and in one case for several days after the fever had ended. This is conclusive proof that there is an abnormal destruction of protein in typhoid fever, and the evidence indicates that this is due chiefly to the toxins of the disease. Shaffer and Coleman were able to demonstrate that this toxic destruction could be prevented or masked by the administration of very large amounts of food, particularly carbohydrates. Kocher[70] has recently shown that in fever even with large amounts of food the nitrogen excretion can never be reduced to the low point of 3 to 4 grams a day readily obtained in health.

In the early days of convalescence from typhoid the metabolism is slightly below the normal, then it rises to 15 to 20 per cent. above, apparently as the result of the large amounts of food and the stimulus of growth. In convalescence the specific dynamic action of food is either normal or else greater than normal. We do not care if the heat production at this period be increased and there is no contra-indication from the metabolic standpoint to liberal feeding in convalescence.

The problem of the mechanism of the rise and fall in body temperature in fever has been the subject of much experimentation, and the question can be settled only by a respiration calorimeter. For reasons that cannot be discussed in a short paper the technic is difficult, and there are only 11 of the calorimeter experiments in typhoid which meet the rigid requirements. These indicate

that a rising temperature is accompanied by an increasing heat production which outweighs a slightly increasing heat elimination. With a falling temperature the production remains fairly level while the elimination is increased.

ANEMIAS. The question of the oxidative processes in cases of severe anemia is of particular interest. When the hemoglobin content of the blood is greatly reduced it is difficult to see how the tissues can be supplied with enough oxygen, and yet every clinician has seen patients with 20 to 30 per cent. of the normal percentage of hemoglobin who are not dyspneic. How is this possible? The blood volume is not increased enough to account for the compensation, the plasma can carry only small amounts of oxygen, the hemoglobin in anemia does not possess an abnormal power to combine with extra amounts of oxygen. Some experimenters have believed that the oxygen requirement in such patients was lower than normal.

The respiratory metabolism in various types of anemia has been studied by Magnus-Levy,[71] Kraus,[72] Bohland,[73] Thiele and Nehring,[74] Grafe,[75] and six cases of pernicious anemia have been observed in the Sage calorimeter by Meyer and the writer.[76] In few cases examined by investigators I have named was the metabolism below normal. In lymphatic leukemia it was often 50 per cent. above normal, perhaps on account of the abnormal oxidative activity of the white blood cells, perhaps on account of lactic acid formation. In two severe cases of pernicious anemia at Bellevue Hospital with 20 per cent. hemoglobin the metabolism was 24 and 39 per cent. above normal.

The chief compensatory factor in such patients would seem to be an increased cardiac output per minute. It appears also that the blood is more completely robbed of its oxygen in its passage through the capillaries.

CARDIORENAL DISEASE. The previous works on the gaseous exchanges in cardiac and renal disease have not been extensive and have been marred by respiratory quotients which are so low that it has been necessary for the investigators to assume abnormal processes. Peabody, Meyer and Du Bois[77] have studied 16 patients in the calorimeter, a number which is somewhat small when we consider the variations present in these diseases. In general it may be said that mild cases of nephritis and compensated cardiac patients are within normal limits, as are a few severe cases of both diseases. An increase in heat production amounting to 30 to 40 per cent. is found in most of the very dyspneic patients. The cause of the rise may be in part the increased work of respiration and increased labor of the heart, but the chief factors are yet to be discovered.

There is no evidence of profound changes in the intermediary metabolism in cardiac and nephritic dyspnea. Not a single ab-

normal quotient has been found by the calorimeter. We must remember that the patients with high metabolism use up more food than normal men, and with ordinary diet will suffer from partial starvation. If not given large amounts of carbohydrate in the food they will subsist chiefly on fat and protein derived largely from their own tissues. It is worth while to remember these things when we order the restricted diets which seem necessary in many cases of cardiac and renal disease.

Miscellaneous Conditions. Many other diseases have been studied in various clinics, but it is impossible to discuss them at length. Grafe[78] has found an increase in metabolism in cancer and only a moderate increase in low-grade fevers. Various diseases of the pituitary have been studied by Falta[64] in Vienna, by Means[24] in Boston, and by the Sage staff in Bellevue Hospital.[79] Results are variable and no conclusions can be drawn as to any marked change in the respiratory metabolism except that in acromegaly there is slight but fairly constant rise in heat production. The metabolism of women just before and just after childbirth was studied most carefully by Carpenter and Murlin[80] using one of the calorimeters in Benedict's laboratory. The effect of drugs on the heat production of men has been studied by Loewy,[81] Lindhard[82] and others and important work is now being done on this subject by Edsall[83] and Higgins and Means.[84]

We must not forget that much of our knowledge of the respiratory metabolism in disease is due to the work done on animals and normal men. We need only mention the researches in this country of Lusk, Benedict, Murlin, Carpenter and many others.

General Considerations. We have seen that the respiration calorimeter measures the heat production by the independent methods of direct and indirect calorimetry. The direct method must remain the standard in the long run and any significant and consistent divergence of the indirect method in any particular disease would indicate a marked change in the intermediary metabolism. It would show that the food-stuffs were not broken down to the same end-products with the same liberation of heat as in normal subjects. Such changes in disease have often been considered very seriously, particularly by investigators who, on account of defective technic, have obtained abnormally low quotients. The calorimeter has obtained no such quotients except in severe diabetes, where they are to be expected. The direct and indirect calorimetry have agreed very closely when we consider the technical difficulties in short observations with sick patients. Until a very few years ago no one would have dreamed of trying to make the two methods agree in periods shorter than six hours. At that time the calculations were not even carried out, but if we now go over some of the work in Benedict's laboratory[80] as early as 1911 we find excellent agreement in two-hour subdivisions of four-hour experiments. With the

Cornell calorimeter built by Williams,[9] Lusk has been able to obtain remarkable agreement in periods as short as an hour with dogs and a dwarf. Howland[31] has obtained similar results with babies. When the totals obtained on all the normal controls studied in the Sage calorimeter are compared it is found that the two methods agree within 0.2 of 1 per cent. With the experiments two to three hours long, such as are used with patients, certain technical errors have a tendency to make the direct calorimetry too low, and we find it 2.2 per cent. lower in typhoid fever, 2.8 per cent. in exophthalmic goitre, 2.3 per cent. in diabetes, 3.3 per cent. in anemia, 1.9 per cent. in the group of cardiac and nephritis patients. These divergences are within the limits of technical error; they are so small that we can be certain that the law of conservation of energy holds good in disease and can also be sure that there are no profound and unsuspected changes in the intermediary metabolism. It is not possible to rule out small changes which might be concealed by the limits of technical error. The chief function of the calorimeter has been to show that the principles of indirect calorimetry are correct when applied to disease. Another function is to make it difficult for overenthusiastic theorists to promulgate wild hypotheses.

The results of work with calorimeters and other types of respiration apparatus must build the foundations of our theories of the nutrition of patients. If we desire to administer to any given patient his exact requirement it is necessary to make several experiments on the patient himself. It is very doubtful if the most experienced observer can guess the heat production of a sick man within 20 per cent. Still, it is possible to make rough calculations which will allow the physician to reckon out the caloric requirements of his patients somewhat more exactly than the trained nurse. We can use as a standard the basal requirement of healthy men between the ages of twenty and fifty and add 10 per cent. for the stimulation of food and about 10 per cent. for the usual activity of a patient confined to bed. Under these conditions the food requirement for the day would be 1800 calories for a man of 125 pounds, 2000 calories for 150 pounds, and 2200 calories for a man of 175 pounds. Bearing in mind the numerous factors already discussed we can add the various percentages according to the disease and its severity. If the patients are permitted to get out of bed, or if they are very restless, we must allow for an increase of anywhere between 20 and 100 per cent. during the hours when they are moving about.

Some observers have attempted to determine the total food requirement in disease by observing the intake and output of nitrogen. Such experiments in nitrogen equilibrium must be continued for weeks to give much evidence on this point. The work at Bellevue Hospital in typhoid fever[38] has shown that a negative

nitrogen balance may exist when the caloric needs are more than covered by the food.

In many cases the fluctuations of body weight serve as a guide to the nutritive condition of the body. We must not place too much reliance on short observations. Rapid changes in weight are due in great part to changes in the water content of the body. Benedict[2] quotes the case of a football player who lost 14 pounds in a game one hour and ten minutes long. Only one-quarter pound was due to the oxidation of solids, 13¾ pounds was water loss. We are familiar with the retention of large amounts of water in edema and are familiar with the role of salts, but we do not realize the frequency of invisible edema. A diet rich in carbohydrates causes the body to retain considerable amounts of water; a fat diet has the opposite effect.

Many clinicians are in the habit of measuring the fluid intake and urinary output under the impression that they are determining the water balance. Patients in the calorimeter eliminate water through skin and lungs at a rate which varies between ½ and 1 liter a day. The fluids of the diet form but a small part of the water intake. Rennet, a solid food, contains just as much water as milk. Potatoes are 75 per cent. water, tomatoes 94 per cent. An accurate water balance is one of the most difficult problems in experimental metabolism and we must not place too much reliance on changes in weight unless followed for long periods.

In reviewing the subject of metabolism in disease one can see that clinicians too long contented themselves with urinalyses and measurements of intake and output. Now they are thinking in terms of the blood and the fluids which bathe the cells. It is certainly worth while to go one step farther and study more closely the respiratory metabolism which tells of the results of the activities in the tissues themselves.

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A NEW CLASSIFICATION OF NEOPLASMS AND ITS CLINICAL VALUE.[1]

By Wm. Carpenter MacCarty, M.D.,
MAYO CLINIC, ROCHESTER, MINNESOTA.

I take the liberty of presenting a new classification of neoplasms[2] for the following reasons:

1. It has been clearly demonstrated that carcinoma in three different organs arises from the regenerative cells of the parenchyma of the organs and not from the parenchyma of these organs (breast, skin and prostate).[3]

2. It has been definitely established that cancer cells of different organs of different germinal layer origin are often morphologically indistinguishable.[4]

3. It has been definitely shown that even the best pathologists cannot always differentiate carcinoma from sarcoma, the cells being often morphologically indistinguishable.

4. It may be seen from the writings of many authorities who classify tumors that their classifications are based on the histogenesis of tissues, and that many of these authorities express dissatisfaction with this basis of classification and apologetically accept it as the best, under the existing state of our knowledge.[5]

[1] Read before the Section on Pathology and Physiology of the Sixty-sixth Annual Session of the American Medical Association, San Francisco, June, 1915.

[2] This brief statement of a biological conception of neoplastic cytological processes serves merely as a preliminary report and is presented at the present time for the purpose of stimulating pathologists and clinicians to study their early neoplasms and chronic inflammatory conditions in the light of the process of tissue regeneration. It also serves to point the way to the standardization of histological and cytological facts with clinical experience.

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5. A review of embryological facts relative to the histogenesis of the different tissues of the body clearly reveals a lack of definite information relative to the exact origin of many tissues, a fact which places any classification which is founded on the histogenesis of tissues on a theoretical basis.[6]

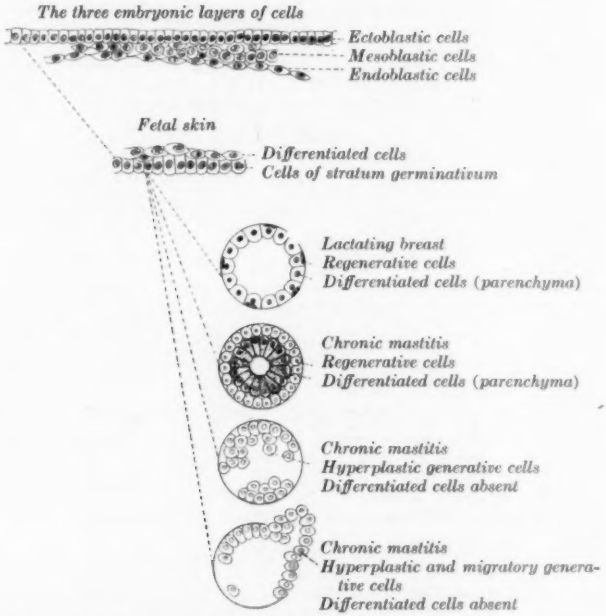

FIG. 1.—Diagrammatically shows the embryonic origin of the cells which comprise the mammary acinus and their activity under the influence of the chronic stimulus or stimuli in chronic mastitis and mammary carcinoma.

6. The histogenetic basis for a classification of tumors is also based on the theory of specificity of tissues which finds some contradiction in biological experimental facts and in certain embryological developmental facts.[7]

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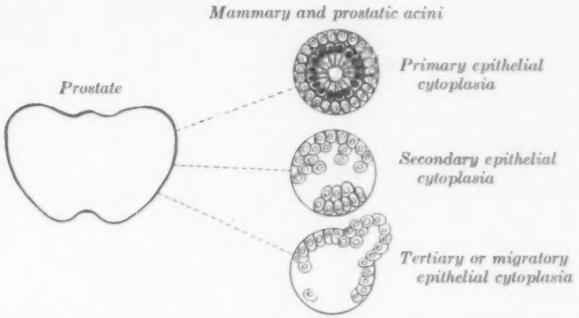

FIG. 2.—The prostatic epithelium presents the same arrangement of cells with the same biological characteristics which are found in the breast.

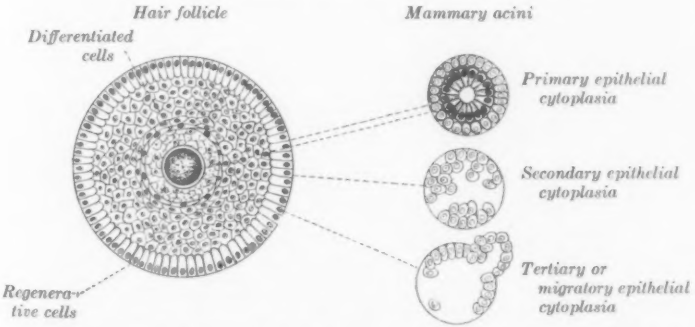

FIG. 3.—The principal cytological changes which occur in the hair follicle in chronic folliculitis are seen in the germinal cells which present the same characteristics which are seen in the mammary acini when undergoing a condition of epithelial hyperplasia.

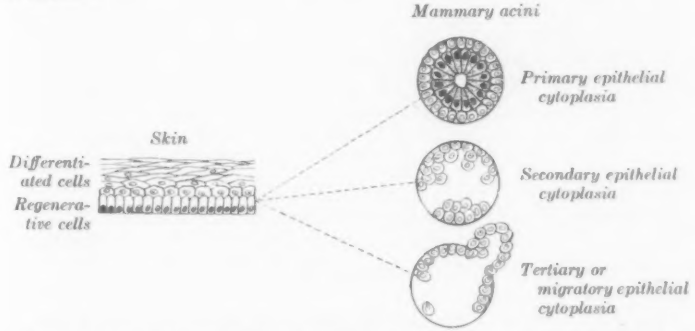

FIG. 4.—In conditions of chronic dermatitis one finds the most marked cytological activity in the germinal layer of cells which present the same characteristics, which are seen in the secondary and tertiary epithelial hyperplasia in the acini of the mammary gland.

7. The classifications which are utilized today by the best authorities do not describe the condition of the cells of tumors but merely name the tumors from the tissues from which they are supposed to, but probably do not, arise.

The classification herewith presented is based on the following established biological facts:

1. The cell is the recognized unit of life.
2. Tissues are communisms of specific or differentiated cells.
3. Organs are communisms of tissues.
4. The fertilized ovum by a process of segmentation produces cells which produce cells, which become differentiated into tissues.

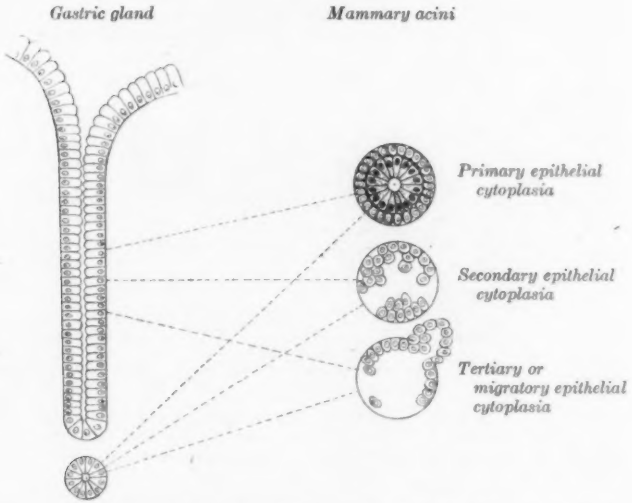

FIG. 5.—The analogy between the observations of epithelial hyperplasia in the breast and those in the stomach. The location of the germinal cells in the gastric gland is at present uncertain. In the gastric gland two rows of cells are not seen as in the prostate, breast, skin and hair follicle. However, where the differentiated columnar or cuboidal gastric epithelial cells are normally present, one sees, in chronic inflammatory conditions, certain cytological pictures, which are analogous to those which are seen in secondary and tertiary epithelial hyperplasia in the breast.

5. During the process of the production of cells which produce tissues, certain cells remain in a stage of reserve (regenerative cells) for the purpose of producing specific tissues when the specific tissues are destroyed.

6. In the presence of chronic irritation, specific cells of tissues are destroyed, the reserve cells become hyperplastic, and sometimes in the presence of failure to reproduce specific cells they form an overgrowth, the cells of which sometimes migrate into the stroma.

7. The cytological process of attempted regeneration expresses itself histologically in three definite stages or conditions: (*a*) by the presence of the atrophic or degenerating specific or differentiated cells plus hypertrophic regenerative cells (primary cytoplasia); (*b*) by the absence of specific cells plus the presence of hypertrophic and hyperplastic regenerative cells (secondary cytoplasia); and (*c*) by the absence of specific cells plus the presence of hyperplastic regenerative cells plus migration of the hyperplastic regenerative cells into the stroma, lymphatics, neighboring and distant organs (tertiary or migratory cytoplasia). (See Figs. 1 to 7.)

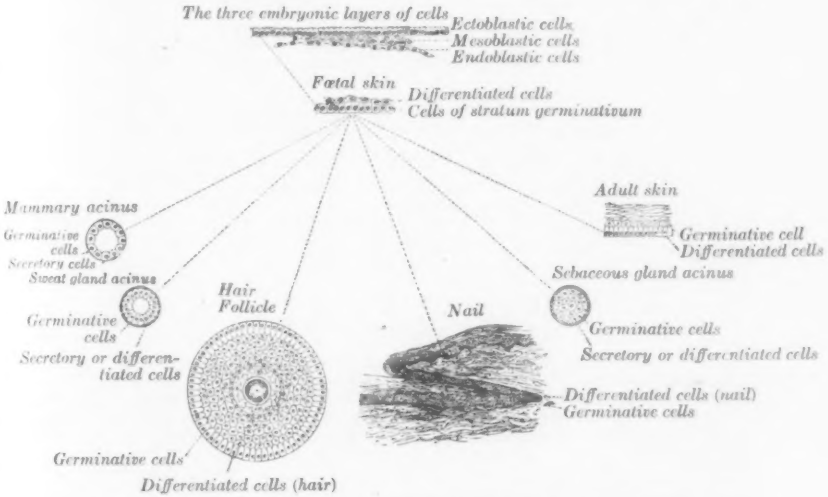

FIG. 6.—Organic differentiation of the ectoblastic cells. The ectoblastic cells become differentiated into the cells of the stratum germinativum of the embryonic skin. The cells of the stratum germinativum become further differentiated into the germinal cells of the mammary glands, sweat glands, sebaceous glands, hair, nails and epidermis. The germinal cells of these organs become further differentiated into the milk-producing cell of the breast, the sweat-producing cell of the sweat gland, the fat-producing cell of the sebaceous gland, the hair of the skin, the nails of the skin and the epidermis of the skin.

8. The first cytoplasia (primary cytoplasia) represents a condition which is commonly accepted as a clinically benign condition. The third cytoplasia (tertiary or migratory cytoplasia) represents a condition which is commonly accepted as a malignant clinical condition. The second cytoplasia (secondary cytoplasia) with our present knowledge is still doubtful as to malignancy or benignancy and represents a group which has been variously considered by both pathologists and clinicians—a group which has caused endless confusion to the pathologist and clinician.

9. Biologically certain regenerative cells react to irritation which destroys the end-products of their specific differentiation: (1) by hypertrophy, (2) by hyperplasia, and (3) by migration.

The terminology of the classification which is herewith presented consists of well-known and accepted terms. It expresses in its first word the stage of cytological activity in response to irritative stimuli; the second word denotes the tissue the regenerative cells of which are involved in the neoplastic condition; the third word is merely a term which signifies condition of cells. Thus by such

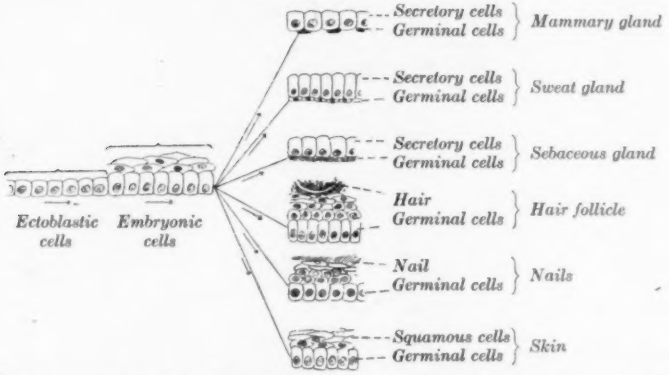

FIG. 7.—Cytological differentiation of the ectoblastic cells. The ectoblastic cells become differentiated into the cells of the stratum germinativum of the embryonic skin. The cells of the stratum germinativum become further differentiated into the germinal cells of the mammary glands, sweat glands, sebaceous glands, hair, nails and epidermis. The germinal cells of these organs become further differentiated into the milk-producing cell of the breast, the sweat-producing cell of the sweat gland, the fat-producing cell of the sebaceous gland, the hair of the skin, the nails of the skin and the epidermis of the skin.

an expression as primary fibrocytoplasia is meant that there is a condition of primary reaction of the regenerative cells of fibrous connective tissue.

In a primary reaction there is an attempted if not complete reproduction of the specific cells. In a secondary reaction there is a failure to reproduce specific cells plus an overgrowth of regenerative cells. In the third reaction there is a migration of the hyperplastic regenerative cells. Each one of these cytoplasias is expressed by terms the etymology of which is well known and accepted in biology. Thus:

I. Primary (restauro-) . . .	fibro- myxo- lipo- leiomyo- rhabdomyo- epithelio- adeno- neuro- lympho- chondro- osteo- myelo- glio- endothelio- perithelio- melano- erythro- poly- x-	cytoplasia.
II. Secondary (expando-) . . .	fibro- myxo- lipo- leiomyo- rhabdomyo- epithelio- adeno- neuro- lympho- chondro- osteo- myelo- glio- endothelio- perithelio- melano- erythro- poly- x-	cytoplasia.
III. Tertiary (migro-)	fibro- myxo- lipo- leiomyo- rhabdomyo- epithelio- adeno- neuro- lympho- chondro- osteo- myelo- glio- endothelio- perithelio- melano- erythro- poly- x-	cytoplasia.

The term polycytoplasia is utilized to express a neoplastic condition in which all or many of the tissues are present, such as in teratomas and dermoids.

The term x-cytoplasia is the convenient term for grouping cytoplasia, the tissue origin of which is unknown.

CONCLUSIONS. 1. This classification, which is in accord with biological terminology and conception, standardizes the science of neoplasia and allows complete correlation of clinical observation with cytologic activity.

2. It forms the basis of an accurate determination of the clinical value of pathological data.

3. It will eventually expel the clinician's pessimistic idea of the work of the histopathologist, who by means of his lack of standardization has certainly incurred severe and detrimental criticism.

SAPHENOPERITONEAL ANASTOMOSIS FOR ASCITES.

BY BERTRAM M. BERNHEIM, M.D.,

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WHEN Ruotte,[1] in 1907, suggested that ascitic fluid be drained off into the general circulation by means of a union between the saphenous vein and the peritoneal cavity, he provided a method of exit not only medically sound and mechanically correct, but one quite feasible as well. It may be theoretically more advisable to prevent the occurrence of an ascites by providing a collateral circulation which will relieve the congested portal apparatus—as carried out in the Talma operation—but the building of such pathways is never certain of accomplishment even under the best of circumstances. Furthermore, the results obtained in those cases in which trial has been made with this end in view leaves much to be desired—the operation either fails of its purpose entirely or only partially succeeds—and not infrequently the patient succumbs in the attempt.

It is unnecessary to discuss the many other measures which have been suggested for the relief of this distressing malady, since most of them have been too theoretical for practical purposes and all of them have been tried and found wanting, except possibly in a very few selected instances. The crux of the matter then is about as follows: an individual, for one cause or another, suffers an obstruction to his portal circulation which results in the pouring out of a tremendous amount of serous exudate into his peritoneal cavity from which it cannot be absorbed. Simple as it is to relieve him of this collection by tapping, it can readily be seen that con-

[1] Saphenoperitoneal Anastomosis for Ascites, Lyon Médicale, 1907, No. 40; Semaine Méd., 1909.

tinuous tappings over a lengthy period will not do because the organism cannot withstand the great loss of fluid thus suffered. The problem then is how to restore this fluid to its normal channels. Routte suggested the use of the saphenous vein, and his method of procedure was to dissect it out for a distance of a few inches from the saphenofemoral opening, cut it in two at the lowest point, tie off the distal end and turn the proximal end up toward the abdomen. Having undermined the subcutaneous tissues overlying Poupart's ligaments, he made an incision through the skin, fascia, and abdominal muscles, drew up the peritoneum, cut a small hole in it to correspond with the opened end of the saphenous vein and did an anastomosis between the two. He suggested that the procedure be done on both sides at one or two sittings, as most convenient.

About twenty-five[2] of these cases have been reported, all, so far as I am aware, having been done abroad.[3] No attempt at special selection of cases[4] was made and the operators[5] had no unusual skill in bloodvessel suturing, yet the result was most promising, since in about one-half a marked improvement was secured. In some instances patients who had been bed-ridden were enabled to resume their occupations. Why a more general use has not been made of the procedure or what results a wider trial would bring forth cannot be surmised. The operation can be done with impunity, lends itself readily to local anesthesia, and causes little or no shock.

Case Report.—The case I wish to present was as follows: Mr. M., aged sixty-eight years, referred by Drs. Omar Pancoast and Frederick Leitz, had suffered from ascites for over a year, the cause being an obstruction of the portal vein consequent on a cirrhosis of the liver. Dr. Pancoast had done a Talma operation some months previously without relief. Repeated tappings were the order of the day, at each tap several gallons of fluid being removed. The depletion thus suffered, the rapid reaccumulation of fluid and the hopeless aspect of his condition in general finally began to tell on the patient to such an extent that he was willing, he even pleaded that something be done that promised possible permanent relief.

Accordingly, on April 25, 1915, under local anesthesia, I exposed the patient's left saphenous vein for a distance of about six inches and cut it off at the lower end of the wound, tying off both ends (Fig. 1). Fortunately for our purposes a large inguinal hernia was present, so it was quite simple to expose the peritoneal sac through a two-inch incision just over the external ring, at which point a very

[2] Morosawa, A. J., Die Ruottische Operation bei Ascites, Centralbl. f. Chir., 1913, No. 4.

[3] Simon, Ueber Ruottische Operation, Berl. klin. Wchnschr., 1913, No. 32.

[4] Schwarzman, Zur Chirurgischer Behandlung des Ascites, Deutsch. Ztschr. f. Chir., Bd. cxxiv, H. 5 u. b.

[5] Permioff-Kasan, Centralbl. f. Chir., 1913, No. 1.

small hole (about 1½ cm.) was made and the greater part of the ascitic fluid that was present—two gallons—was drained off (Fig. 2). This done, the tissues overlying Poupart's ligament were undermined by means of a curved clamp, and the proximal end of the severed vein pulled up into the small incision, where a lateral anastomosis was done between the bloodvessel and the peritoneum, ordinary bloodvessel silk (No. 00000) being utilized (Figs. 3 and 4).

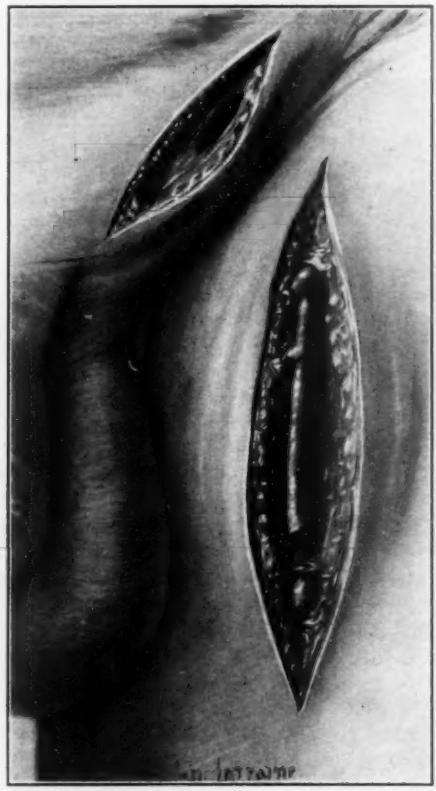

FIG. 1.—Saphenous vein exposed. Its distal end ligated.

Prior to the suture it was noted that the vein valves were competent—that is, allowed no back bleeding. And the patency of the vein lumen was definitely established by running a few cubic centimeters of salt solution through it into the general circulation by means of an ordinary Record syringe. The only disturbing feature was the apparent small caliber of the vein, it being only

about one-half normal diameter, although its wall was quite soft and normal in every respect.

A lateral anastomosis—accomplished without great difficulty—was preferred to the usual end to side because of the greater ease of operative performance. Both wounds were closed in the usual

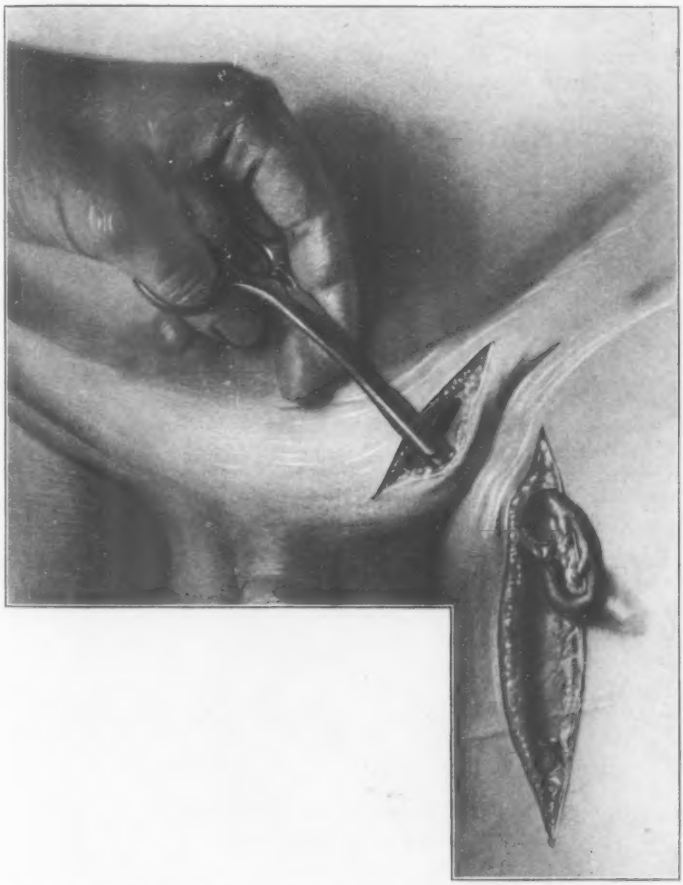

FIG. 2.—Incision through peritoneum. Vein being pulled through undermined fascia.

manner and the patient left the table in good shape. It had been my original intention to do both sides at one sitting, but owing to the patient's great age and poor physical condition, and the fact that the right leg was markedly edematous, it was deemed best to do but the one.

For twenty-four hours all went well, but the patient insisted on getting on his feet to urinate—as had always been his custom—and the result was leakage at the site of the suture, probably due

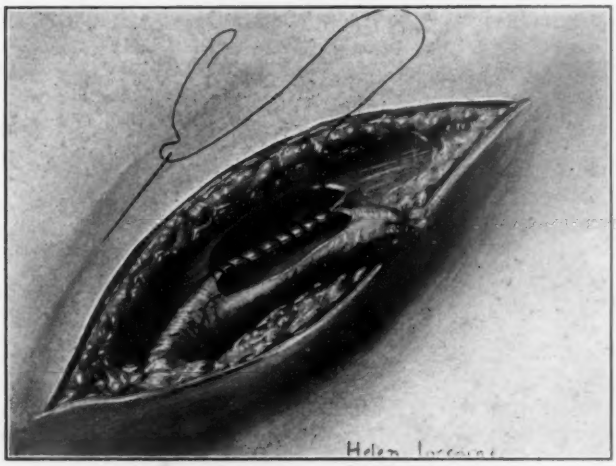

FIG. 3.—Peritoneum and vein being united.

to the great strain put upon it, since all of the ascitic fluid had not been withdrawn. This leakage continued for two or three days, until finally I compelled the patient either to be catheterized or to

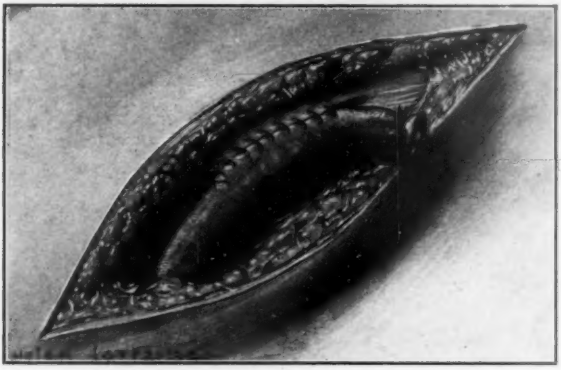

FIG. 4.—Anastomosis completed.

pass his urine in the recumbent position. He did the latter, and, the foot of the bed being elevated, the leakage promptly ceased. Thus matters progressed, temperature but slightly elevated, wound

in good shape, and patient apparently in good condition, until midnight of the eighth day, when he complained of pain in his right shoulder. He had had similar pains in this shoulder frequently before coming into the infirmary, so but little was thought of the matter, and he was given a hypodermic injection of morphin, gr. $\frac{1}{6}$. Early next morning he was given by hypodermic $\frac{1}{8}$ gr. of morphin, and an hour or so later, his pain being still unrelieved, this was repeated, when by chance his nurse found a small bottle of morphin tablets (gr. $\frac{1}{4}$) under his pillow. Questioned as to where he had gotten them, he said they had been given to him some weeks previously by his physician, and he had been in the habit of taking an occasional one as needed. He claimed that he had not taken any of the tablets during this last attack of pain, but whether he did or not the fact remains that gradually during the morning he went off into a semiconscious stuporous state from which he could be aroused with difficulty. His pupils were a bit contracted, he was rather cyanotic, and seemed to have a certain degree of air-hunger. A careful examination failed to reveal the slightest degree of dilatation of the heart. In fact, no cause whatever could be found for this patient's death, which took place about sixteen hours after the initial attack of pain in his right shoulder. His bowels had been in good shape and he had been voiding, apparently, a sufficient amount of urine. Whether this was a death from morphin poisoning or not cannot be told with certainty. It does not seem possible however, that the man died from his operation. There was no symptom of an embolus nor was a demonstrable pneumonia present.

The family refused permission to do an autopsy or even an exploration at the site of the wound, although every effort was made to secure this permission, and all sorts of influence brought to bear. This was most unfortunate, since considerable light might have been thrown on the case and valuable knowledge for future guidance might thus have been secured. It seems fair to conclude, though, that the operation is worthy of further trial in suitable cases, since technically it is not difficult to carry out, and theoretically it has much to commend it.

THE THERAPEUTIC POSSIBILITIES OF ANTITETANUS SERUM.

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(From the Pathological Institute, University of Freiburg in Br., Prof. L. Aschoff, Director.)

It is a generally recognized fact that tetanus antitoxin may be employed in two ways: (1) as a prophylactic measure, having for

its object the prevention of a possible outbreak of tetanus,[1] and (2) as a therapeutic agent for combating the toxin of this disease after symptoms have already appeared. While these two divisions of the subject each require special consideration, it must be recognized at the outset that the principles which underlie both applications of the serum are exactly the same.

In both we are concerned with a foreign serum which when injected into the body, no matter whether under the skin or into the cerebrospinal canal, in a comparatively short time is absorbed from the tissue spaces into the blood stream, from which in turn it is later partly distributed to the general lymph circulation and partly excreted. Knorr found in animal experiments that the maximum amount appeared in the blood stream twenty-four to thirty-six hours after subcutaneous injections. From that time the amount steadily decreased until on the sixth day only about one-third and on the twelfth day one fifty-fifth of this quantity was present, while at the end of three weeks none at all could be demonstrated. Behring showed that after injecting a definite amount of tetanus antitoxin into the blood stream this amount remained practically unchanged for about one hour, after which time it gradually began to decrease. Indeed so confident was he of this retention of antitoxin in the blood stream that he proposed that such injections should be used, both in man and in animals, as a means of determining the amount of blood in the body. The value of this new method has been repeatedly confirmed, among others by Zangemeister, Matthes, Friederick v. Müller, and Kämmerer and Waldmann.

The disappearance of antitoxin from the body follows in general those laws which govern the disposal of any foreign serum *in vivo*. Behring was able to demonstrate its presence in the urine and intestinal secretions of passively immunized guinea-pigs, and Vagedes claimed to have found it in the urine of a man who had been treated with antitoxin. Brieger and Ehrlich investigated the milk of nursing animals which had received injections of serum, and discovered that appreciable quantities might be excreted in this manner. Tizzoni and Cattani, among others, have shown that it is able to pass through the placental bloodvessels in a preg-

[1] One must not, however, confuse prophylaxis in tetanus with, for example, vaccination in smallpox or typhoid fever, which, while they are also prophylactic or protective measures, depend entirely for their protection upon reactions which occur, *intra vitam*, between the vaccine and the tissues and fluids of the body, by which reactions newly formed protective substances are produced which are capable of warding off the diseases for which they are specific. The protection afforded by such vaccines often lasts for years. Tetanus antitoxin, on the other hand, the same as diphtheria antitoxin, is a finished product, capable of at once neutralizing its specific toxin no matter whether the contact between the two occurs within the body or *in vitro*. As would be expected the protection obtained from such a serum is comparatively transitory. This phase of the subject (prophylaxis) has been fully treated in a previous article.

nant animal and can then be demonstrated in the blood of the offspring. Undoubtedly a considerable amount is destroyed in the body, this destruction probably taking place both in the blood stream and in the tissue fluids. The phenomena associated with so-called "serum Krankheit," or anaphylaxis, are supposed to depend upon the action of a ferment which is capable of splitting up the antitoxin molecule. In a case of myelogenous leukemia, Kämmerer and Waldmann noted that it disappeared more rapidly than usual from the blood, due, as they suggested, to the increased tryptic activity of the leukocytic ferments.

Naturally in the disposal of this serum the lymph plays an important role. Ransom was able to find traces of antitoxin in the ductus thoracicus of a dog a few minutes after intravenous injection, and also showed that while it was later present in the cerebrospinal fluid and nerve lymph the amounts were always less than those in the blood stream. As would be expected the proof of its presence or absence in the tissue spaces of the brain and spinal cord is exceedingly difficult, because the well-known antitoxic properties of these tissues themselves would obscure the results of any of the usual test methods. However, it is reasonable to suppose that since it passes over into the lymph stream and is present in the cerebrospinal fluid and nerves it must also penetrate to the tissue spaces of the brain and cord if only to a limited extent.

When tetanus antitoxin, then, is injected into the body by the subcutaneous or intralumbar methods it is rapidly absorbed into the blood stream and the processes of excretion and destruction cause it to disappear entirely from the body in a few weeks. By intravenous injections, on the other hand, it is more rapidly distributed throughout the entire body and also more quickly passes from the blood into the general lymph circulation. Its greatest concentration, however, excepting only the local point of injection, is always in the blood stream.

Having reviewed the conditions under which tetanus antitoxin remains in the body, we are better prepared to consider its employment in the cure of tetanus after symptoms have once appeared, *i. e.*, its therapeutic possibilities.

In an attempt to reach a correct judgment of the value of tetanus antitoxin as a therapeutic or curative agent, the pendulum of both experimental and clinical medicine has swung from one extreme to the other. One naturally expected at the outset that its effect on the mortality of tetanus would be equal to that of diphtheria antitoxin on the mortality of diphtheria, and Behring confidently predicted that provided the serum was given early enough (within thirty hours after the first symptoms appeared) and in large enough doses (100 units, German standard) the death rate could be reduced to as low as 15 to 20 per cent. It is not our purpose to review here the statistical evidence on this question. One needs

only to consult the extensive reports of Steuer, Engelmann, Köhler, Lemonnier, Vallas, Chattot, Jacobson and Pease, Ullrich, Permin, and others to form a fairly accurate estimate of the results of the study of large collections of treated cases. Certainly the earlier expectations have not as yet been realized and the general clinical opinion in this regard is today decidedly pessimistic.

In the laboratory and on the theoretical side the same differences in results and opinions have appeared. Knorr by carefully graduated doses of tetanus toxin and antitetanus serum was able to save the lives of laboratory animals by beginning treatment as late as thirty-six hours after the injection of toxin and twenty-four hours after the appearance of the first symptoms. In order to meet the possible objection that the injection of artificially prepared tetanus toxin does not compare with the conditions of natural infection, he also used splinters of wood inoculated with tetanus spores, and by placing these under the skin of guinea-pigs he could still save their lives by the use of repeated large doses of serum given first as late as four days after the inoculation and thirty-six hours after the first symptoms had appeared.

These results have not been confirmed by the researches of most other workers. For example, Roux and Vaillard as well as Beck were unable to save animals if the treatment was not started before symptoms first appeared. Also in my own earlier experiments, which were directed toward establishing the therapeutic value of antitoxin, the results were fully as discouraging. As a rule it was necessary to give antitoxin under the skin at least two hours before the injection of toxin if we would save the animal's life. In the very occasional cases in which antitoxin was given first after symptoms of tetanus appeared, and the animal survived, the symptoms were always slow in advancing toward the upper parts of the body, *i. e.*, they were for a comparatively long time confined locally to one or both hind legs.

Hence it becomes very important in this connection to keep in mind the differences between laboratory and human tetanus. Most of the laboratory animals (guinea-pigs, rabbits, rats, mice, etc.) after a subcutaneous or intramuscular injection of tetanus toxin or inoculation of tetanus spores in the hind leg show a local tetanus or "tetanus ascendens" (Zupnik), *i. e.*, the toxin is first and in large part taken up by the lymph channels of the motor nerves of the inoculated extremity and thus conveyed to the corresponding centres in the spinal cord, from the poisoning of which centres entirely local spastic phenomena are first produced. It is not until many hours (twelve to twenty-four) later that the centres governing the opposite limb and those lying higher in the spinal cord become affected, and only after the lapse of several days do the respiratory levels begin to show evidences of intoxication. In fact, in these animals the vital centres are usually the

last to suffer attack. For some unknown reason the main path of travel for the toxin is up the spinal cord, and only relatively small amounts of toxin appear to be distributed by the blood stream to the other motor nerves of the body.[2]

This peculiar reaction is largely a property of certain animal species, not being shared by all animals alike, *e. g.*, the frog never shows local tetanus (Gumprecht). It probably depends upon the movements of the lymph currents in the nervous system and their relation to the capillary blood circulation of the muscles, as well as the varying degrees of sensitiveness of the various centres in the spinal cord and brain to the influence of tetanus toxin. By injecting tetanus toxin into the blood stream of a rabbit or guinea-pig, or subcutaneously into the tip of the toe (Zupnik), symptoms more generalized and often approaching in type those seen in man may be produced. Even here, however, the resemblance is only superficial, for not only can toxin be shown to have early invaded the sciatic nerves (Meyer and Ransom), but the spasmodic cramps, at least in the first stages, are much more intensive in the hind-quarters.

In man, on the other hand, no matter where the site of the infection may be located, the first symptom is usually *trismus*, *i. e.*, the motor centres which lie near the most vital centres of the nervous system are the first to be attacked. The further progress of the disease follows that of a tetanus descendens, or, better, a general tetanus, and is comparatively rapid in its development. The toxin, instead of largely passing to the spinal cord by the peripheral nerves of the injured part, is rapidly absorbed into the blood stream, and from this is first conveyed to the nerve centres either directly or by the nerves of the face and neck.[3] Zupnik believed these facts could be explained by the varying reaction between opposed groups of muscles, while Pochhammer suggested that the condition was due to the comparative shortness of the upper spinal nerves, and endeavored to show that, in general, the length of the nerves regulated the time of the appearance of symptoms. The difference exhibited by the various animal species, however, in their reactions to tetanus toxin can hardly be explained on this basis, and I am more inclined to offer the above-mentioned possibility, namely, a varying degree of sensitiveness of the various centres for tetanus toxin.

[2] Meyer and Ransom hold that tetanus toxin, at least in animals, is never directly absorbed from the blood into the central nervous system, but always passes indirectly by means of the peripheral nerves. It is difficult to determine to what extent this holds true. As Permin emphasizes, both the indirect passage through the nerves and the direct absorption from the blood must be granted as theoretical possibilities.

[3] Cases of fairly typical tetanus ascendens or local tetanus are also described as occurring in man, and have been carefully reviewed by Sawamura. Not only are such cases rare, but they are usually mild in their course and symptoms, *e. g.*, of the 12 cases collected by Sawamura, 8 recovered.

From these facts it is clear that the results obtained by the administration of tetanus antitoxin to animals in cases of tetanus ascendens cannot rightfully be used as a measure upon which to judge of the exact treatment required and justified in human cases. In laboratory animals not only is the toxin in the blood neutralized, but undoubtedly, in many cases, its advance in the lymph spaces of the nerves and spinal cord can be brought to a standstill. This latter result is probably also influenced by the fact that the chemical combining power, which fixes toxin to the ganglion cells of the spinal cord, in tetanus ascendens, is, at first, largely exerted by the cells in the lower levels, so that the amount of toxin in the early stages is markedly diminished by its union with lower and less vital centres of the cord. On the other hand, in man, when the first symptoms have appeared, the vital centres, as a rule, are already in grave danger, and in a large percentage of cases, especially those with an incubation period under six days, it is very doubtful if any means whatsoever will avail to preserve these centres from attack.

Our main efforts must, then, be directed toward the neutralization by antitoxin of the toxin which is present in the blood stream, and that which may be further produced and thrown into the blood.

One can hardly hope in man to overtake and render harmless that toxin which is already in the lymph channels of the nerves or the lymph spaces of the central nervous system or that portion which has become united with the nerve cells and has brought about the initial symptoms. Theoretically if one could inject antitoxin into each of these nerves or into the threatened regions of the cord and brain the small percentage of toxin still present in these lymph spaces might be neutralized; practically such measures are, of course, absolutely out of the question. The injection of nerves in the injured extremity, such as the sciatic, so effective in the local ascending tetanus of laboratory animals, in human beings serves very little if any useful purpose. Such injections do not distribute antitoxin directly to the rest of the spinal cord—they only serve to protect the corresponding centres of those nerves which are injected—and not only are the motor centres of the extremities not vital centres, but their nerves in man are not the most important conductors of tetanus toxin to the cord and brain. The very best one can do is to render harmless, at the earliest possible moment, the toxin circulating free in the blood and to make impossible the circulation of any further toxin. For this purpose the intravenous injection of antitetanus serum is, as v. Graff emphasizes, a nearly perfect remedy, and, moreover, is not demanded in overwhelming or even large doses.

In the endeavor to cure experimental tetanus in animals one aims toward forcing a high concentration of antitoxin into the lymph fluids, toward driving antitoxin into the lymph spaces of

the nervous system—in short, to overwhelm the body with large doses of antitoxic serum with the expectation of preventing the onward march of tetanus toxin toward the threatened centres of respiration. In these laboratory animals such a procedure is also theoretically more or less justifiable, for, as explained, the toxin advances rather slowly from below upward, so that flooding of the body and, thereby, to a certain extent the central nervous system, with antitoxin may be the means of preserving the animal's life. In man, on the other hand, such measures not only serve no useful purpose but are a waste of good antitoxin.[4] This surcharging of the lymph spaces with antitoxin is distinctly a time-consuming process, for the antitoxin molecule, perhaps due to its comparatively large size, does not readily pass unchanged through the excreting and secreting membranes of the body. By the time the nervous system has been flooded it is too late—tetanus toxin, in man, after the appearance of symptoms, is already in the region of the vital centres of the medulla and only a minimal lapse of time suffices for a fatal intoxication.

To overcome this difficulty, several "short cuts" have been proposed. Roux and Borrel suggested that the serum be injected directly into the brain substance. Not only has the method proved to be a dangerous operation, but it has very little rational basis for its justification. In animals, perhaps, for the reasons explained above; in man there is little reason to suppose that it does more than protect its local area from toxin invasion, while the surplus is, in turn, absorbed into the blood stream and then follows the usual path of antitoxin introduced in other ways. It may be freely granted that if the injection could be made into the region of the "danger zone" a certain amount of protection might be effectively produced. However, naturally the danger from the toxin would only be substituted by the equally pressing dangers incident to the injection itself.

Blumenthal and Jacob first advocated intralumbar injection of antitoxin, hoping thereby to exert a more direct and quicker action on the toxin in the nervous system. Here, again, in laboratory animals the procedure was accompanied by good success, and hence found wide acceptance in the treatment of human cases. There can be no doubt that in such animals the method possesses certain advantages over some others, *e. g.*, subcutaneous injections. Gumprecht was able by this means to block off the nerves of the lower extremities so that the corresponding spinal cord centres were protected against the advance of tetanus toxin. Meyer and Ransom confirm Gumprecht's experiments, but they also insist

[4] When, however, for his own peace of mind and with the hardly justifiable hope that the toxin then present in the lymph channels of the nervous system may yet be neutralized, the physician feels that he must resort to a large dose, this should, if it is to accomplish any good purpose, be given intravenously and not subcutaneously.

that the antitoxin so injected is promptly absorbed into the blood stream and has little or no effect on the toxin present in the spinal cord. But, granted that the lumbar level of the cord could thus be protected, this is not the "danger zone," and is far removed from it. Just as with the intracerebral injection, if the antitoxin could be introduced into the cervical region of the spinal column, as suggested by Jonnesco, the slight advantage gained in combating the toxin in the lymph channels of the nerves would be more than counterbalanced by the dangers of the operation.

Permin has proposed as a possible modification of the subarachnoid injection the lowering of the patient's head to as near the vertical as possible, hoping thereby to bring the serum, through the action of gravity, into contact with the cervical nerve roots. In animal experiments this method proved to be a slight improvement over the usual intralumbar injections, but even here it was necessary to give the antitoxin not later than six hours after the toxin in order to save the animals. To say nothing of the doubtful practicability of this procedure in human beings, there would be an evident loss of time in bringing the antitoxin into the desired regions of the subarachnoid space, and it is this loss of time, when every minute may mean a serious difference in the outcome of the case, that we wish by all means to avoid.

Early in his work on tetanus antitoxin, Behring recognized the theoretical advantages of the intravenous injections, but he exhibited a distinct hesitancy toward giving this method his unqualified indorsement. This hesitancy evidently, in part at least, proceeded from a fear of the dangers incident to the injection of a foreign serum into the body and a belief that these dangers were more threatening with intravascular than with subcutaneous administration. It is true that with extensive use of diphtheria antitoxin, cases of "serum Krankheit" became fairly common, and in a small percentage of cases threatening symptoms of asphyxia and even death followed its use. While, however, the occurrence of urticaria and other skin phenomena, following the administration of tetanus antitoxin, is well known, there are, so far as we have been able to find, very few records of "serum death" which really resulted from its use. Not only has the work on anaphylaxis or proteid reactions shown that there is little difference to be observed as regards the method of injecting the foreign proteid, but with the present purification and concentration of modern antitoxic serums this danger has been reduced to a negligible minimum.

On the contrary the subcutaneous method has met with much more favor from the clinical world, and largely because of its simplicity and ease it may be said today to be the one most usually employed. It should be distinctly emphasized that for therapeutic or curative purposes, *i. e.*, after symptoms have appeared, this method is a useless and irrational waste of precious time. All local subcutaneous injections of antitoxin are able fully to protect the

local area from toxin. But our main purpose is not to protect the local area, but to reach the toxin circulating in the blood.

I propose, therefore, that every case in which symptoms of tetanus appear be treated at once, without delay, with an intravenous injection of 3000 units[5] of antitetanus serum. The "at once" should be emphasized. Even the saving of minutes of time may mean the difference between the life and death of the patient. The experiments of Donitz and others show with what exceeding rapidity toxin travels in the body and how soon it passes in part beyond the reach of all antitoxin. It is not believed that by this or any other known therapeutic procedure the lives of all or even of any large proportion of tetanus patients can be saved. Prophylaxis is, as has been shown,[6] the only means known at present which can bring the death rate in tetanus to anywhere near the zero point. It is desired here merely to emphasize that by this method every patient who exhibits the symptoms of tetanus is given the best possible opportunity of preserving his life. Difficult or dangerous surgical operations, such as the intracerebral method or intralumbar injection, need not be considered; the loss of time and local pain of subcutaneous injections are avoided, and, what is of less theoretical, but nevertheless often of more practical serious moment, the use of large amounts of serum is obviated. The method consists simply in the immediate insertion of 3000 units of antitoxic serum into one of the veins of the elbow.[7]

[5] In the work of Aschoff and Robertson twenty antitoxin units (German standard) was suggested as the unit dose for intravenous injection in cases of outbroken tetanus. This amount was more or less arbitrarily fixed. It is, for one thing, in Germany the usual prophylactic dose, and is held in bottles containing exactly this amount. The amount of antitoxic serum which neutralizes an amount of test toxin which would destroy 40,000,000 grams of mouse contains 1 unit of antitoxin by the German standard. In the United States a unit is defined as the amount of antitoxin required to just neutralize 1000 fatal doses of tetanus toxin for a 350-gram guinea-pig. Supposing both mice and guinea-pigs to be equally susceptible per gram weight to tetanus toxin, it may at once be seen that the German antitoxin unit is about one hundred and fifteen times as potent as that of the United States. If we should accept the work of Behring, who states that a guinea-pig is six times as sensitive to tetanus toxin per gram weight as a mouse, then the German unit would be correspondingly greater in neutralizing power. However, the figure 3000 has been selected in this country as representing an approximate equivalent to the original figure.

[6] Robertson, The Prophylactic Use of Tetanus Antitoxin, AMER. JOUR. MED. SCI., May, 1916, p. 668.

[7] In this connection must be noted the theoretical possibility that at the time of the injection of antitoxin there may be no toxin then present in the blood stream. There are many facts which indicate that the formation and absorption of toxin occurs, under usual conditions, in the early days of a tetanus infection, and that then both the presence of granulation tissue and the exhaustion of the bacillus' growth or toxin forming ability greatly diminish or even entirely prevent further entrance of toxin into the blood and lymph streams. Also, Pochhammer claims (p. 683) that "each tetanus patient, either man or animal, at the time of the outbreak of symptoms often already possesses in his blood serum large quantities of antitoxin." If one could be certain in any given case that either of these conditions prevailed, the intravascular injection of antitoxin (or administration by any other method) could have no reasonable purpose. However, not only has little proof been advanced for Pochhammer's assertion, but, on the contrary many times (among others by Nissen, Brunner, Buschke and Oergel, and Symanski) the presence of tetanus toxin has been demonstrated in the blood. On the whole, we must follow those rules in treatment which give the most reasonable expectation of success.

Furthermore it is of little or no value to repeat this dose twice a day or every other day or, in the large majority of cases, at all. The one injection of 3000 units is amply sufficient to neutralize the toxin which might be elaborated and absorbed from any ordinary tetanus infection, and this antitoxin will remain effective in the blood stream for at least one week, *i. e.*, long enough to decide the issue in almost all cases of human tetanus. If the case should become chronic or suffer a recurrence or any other special condition should develop which might indicate the advisability of giving more antitoxin, there can be no objection to a second or even a third dose; but here again it should be emphasized that a small dose is fully as effective as a large one and a large dose is as unjustifiable the second time as it was the first.

In conclusion, I should like to be certain that undue emphasis shall not be placed upon the element of dosage. The proposal is that as soon as symptoms of tetanus have appeared, 3000 units of antitetanus serum should be injected at once into the circulation. The immediate intravascular injection is the important feature and the amount of the dose a purely secondary matter. Personally I am fully convinced, for reasons which cannot be discussed here, that one-half this amount would be just as efficacious. Twice this dose, however, can do no harm. The main stress is here laid upon the recognition of the theoretical considerations which underlie the therapeutic application of antitetanus serum and a rational *modus operandi* based upon these principles.

Naturally the complete treatment of the disease involves the application of many other measures the consideration of which does not come within the scope of this paper, but will be fully discussed in a later article.

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INTESTINAL STASIS.

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The treatment of intestinal stasis can no longer be relegated to the realm of empiricism but demands an individual study of each case, including a careful history—physical, laboratory, and, in many instances, Roentgen-ray examination.

Regarding the history, there are some general points which at first may sound trivial, but which often have a profound bearing on the case. Among these is the mode of living. Many men and women suffer from habitual constipation simply through lack of regular habits; men who commute, eat their breakfast with an eye on the clock and before the last mouthful is swallowed, seize hat and coat and rush for a train. Some young women, either from diffidence or lack of proper hygienic education, never seek the toilet until the demand becomes imperative. The inclination to defecation being resisted, the desire soon passes away and often does not occur again until the next regular period.

It is this voluntary inhibition of defecation, with its consequent retention of feces, that leads to the blunting of the sensibility of the rectum, and is one of the most potent factors in the production of a common variety of stasis.

The human intestines, as a rule, evacuate their contents every twenty-four hours, usually after breakfast, although there are exceptions to this in apparently healthy persons, who defecate at intervals of forty-eight hours to four or five days; but they are the exception. This desire to defecate after breakfast is partly habit, but due more to the stimulus of food entering a completely empty stomach and starting intestinal peristalsis.

The intestinal movements under certain conditions are inhibited by nervous influences. Thus, Cannon found that intestinal movements in cats ceased when they were excited or angry.

Much of the activity of the intestines depends on the chemical as well as the mechanical stimulation of the food, its digestion, and its bacterial decomposition.

Vegetable food is more important than animal, both on account of the mechanical irritation and because of its stimulation through fermentation.

The question in treating any case of stasis is to find out the etiological factor or factors.

A careful history, as has been said, is the first essential. The examination of the abdomen, rectum, stool, urine, and possibly a Roentgen-ray follow as a routine measure.

In examining the abdomen the following points should be especially noted:

The *habitus*, namely, the degree of the costal angle. Such cases presenting the so-called habitus enteroptoticus, with the narrow costal angle and generally poor muscular development, have a tendency to visceral ptosis with its resulting kinks and angulations. Again, such persons are much more prone to constipation than are those with a normal, well-developed habitus, owing to a weakness of abdominal and pelvic muscles.

The former teaching that constipation was the result of colonic atony or spasm is, in the light of more recent work, no longer tenable. Holtzkneck, Hertz, A. E. Barclay, and others have shown that the intestinal propulsion of contents is not a slow, gradual process, but one which they term "mass movements," namely, a sudden forward movement of the entire fecal mass, the action being exceedingly rapid. Holtzkneck has reported an observation where the head of the bismuth column was in the region of the hepatic flexure, and when the movement finished, which took about three seconds, the head of the bismuth shadow had advanced beyond the splenic flexure. This mechanism appears to be: (1) a relaxation of the tonic action of the muscular coats; (2) followed by a big peristaltic wave that sweeps the whole contents along. The movement probably occurs three or four times a day, and it is strongest after breakfast when food is received in the stomach after a night's fast.

Leaving out of consideration the question of kinks and angulations and inflammatory conditions, such as a chronic appendix, we recognize two main types of constipation: (*a*) that occurring in the sigmoid and rectum; (*b*) that occurring in the cecum, which has been termed "true constipation," and is due to a failure of the mass movement.

The former, *i. e.*, rectal constipation, is much more common.

It is highly improbable that the cecum has any part in the forward propulsion of feces. This portion of the gut apparently has a separate mechanism or peristalsis for the mixing of contents and feeding them into the ascending colon preparatory to the occurrence of the "mass movement."

Hertz attributes the dilated splashing ceca to the result of a failure of the forward mass movement, the intestinal contents regurgitating back into the cecum, causing an inflammatory reaction which results in relaxation and absorption of the mucosa and muscular coats, and that such ceca are the results and not the cause of constipation.

The cecal or "wet constipation," as it has been called, is liable to be associated with symptoms of toxemia, while, on the other hand, the rectal and sigmoid type, which has been termed "dry constipation," is rarely associated with any toxic symptoms.

When we come to consider the etiological factors in these types of stasis the whole problem is wrought with many difficulties, for it must be realized that the large intestine is but one part of a complex organization so closely linked together by nerve-centre relays and subcentres that it is almost impossible to separate the constituent anatomical parts and deal with them separately.

Whether these sloppy ceca are the result of faulty mechanics or bacterial infection is still undetermined; the general feeling is one of faulty mechanics, the inflammation and infection being secondary.

Ileal Stasis. In 1903 Arthur Keith demonstrated the existence of a strong ileocecal sphincter in man; he suggested, and his observations have been borne out by others, that the function of this sphincter is to prevent the contents of the ileum from passing too rapidly into the cecum and not, as has been suggested by some observers, to prevent antiperistaltic waves, which do not normally occur in the ascending colon, from passing feces from colon to the ileum.

Alan Newton and Hertz showed that bismuth containing chyme reached the end of the ileum an hour or longer before any appreciable quantity passed into the cecum, and that the ileum is still full four to seven hours or more after the last trace of bismuth has left the stomach, consequently an accumulation of chyme occurs in the last few inches of the ileum, where it remains and undergoes digestion for a longer period than in the stomach; this ileal stasis, up to a point, is a physiological condition.

Normal ileac stasis is increased in all conditions leading to spasm or to the inhibition of the normal relaxation of the ileocecal sphincter.

In acute appendicitis, for example, the sounds which normally indicate the squirting of the contents of the ileum into the gas-containing cecum cease completely, owing, probably, to spasm of the sphincter.

Also an accumulation of feces in the cecum will give rise to back pressure, and in every case of cecal constipation one will see evidence of ileal stasis. Thus the necessity of having the colon well cleaned before attempting to make a radiographic diagnosis of ileal stasis.

Stasis of the terminal ileum can result, according to Lane, from a thickened mesentery band supporting the terminal end of the ileum, while the cecum and remaining portions of the small intestine are allowed to sag in the pelvis.

Lane, as is known, further maintains that the pull exerted by the prolapsed small intestine exercises, through the medium of the

jejunum, a strain on the termination of the duodenum, producing a kinking at the duodenojejunal junction, and giving rise to a partial obstruction at the terminal portion of the duodenum.

It would seem, from numerous radiographic studies, that ptosis of the intestines alone does not lead to stasis, except in rare instances at the splenic flexure, from too acute angulation.

In fluoroscopic examination of the colon it often appears as if there were exceedingly sharp angles at the hepatic and splenic flexures, but this would seem to be due more to the shadow being cast in a single plane, for when viewed from the side they form a wide angle.

Adhesions involving the limbs of the hepatic and splenic flexure can almost always be determined by ascertaining if they can be separated by palpitation during the fluoroscopic examination. I have observed numerous pelvic ceca and transverse colons in patients whose bowels were functionating normally, and in my opinion such cases of ptosis are not in themselves sufficient to cause stasis.

A ptosis of the transverse colon, in my experience, never leads to kinking at the hepatic flexure, although an enlarged and prolapsed right kidney has been known to produce obstruction by pressure at this point.

As a rule, in most cases of constipation, a single part of the bowel, such as the rectum, pelvic colon, ascending colon, or splenic flexure, is involved, and treatment should therefore be directed to that part, and many of these conditions require surgical interference.

In those cases in which the whole colon is involved, medical treatment almost invariably succeeds.

A simple but valuable test for judging intestinal motility consists in giving a few capsules of charcoal and noting how long it takes the coloring matter to appear in the feces. It takes on an average four and three-eighths hours for the feces to reach the cecum, nine hours to the splenic flexure, and eleven hours to the brim of the pelvis. In defecation all the contents of the bowel beyond the splenic flexure are excreted, so that charcoal given eight hours after the morning stools—say about 4 P.M.—would under normal conditions appear the following morning in the feces, or sixteen hours after its ingestion.

Such a test is useful in diagnosing doubtful cases of stasis.

The feces should be examined in every case of constipation. From the gross examination one is able to make a fair estimate as to the amount of elimination and the general character noted —whether it consist of a formed, well-digested cylinder, or if compressed to the "lead-pencil" shape, as is seen when spasm or stricture exist. When the residue has been retained for a long period of time in the pelvic colon it is apt to be lumpy in character, and

may be streaked with blood derived from the irritation of the rectal mucosa.

The existence of a colitis is characterized by the presence of mucus and, at times, undigested food. The mucus may be mixed with the feces or be passed at the same time, having a viscid, glairy appearance; or else it appears in strings or cylinders—the so-called "bowel casts"—resembling strips of wet tissue paper, which characterizes a mucomembranous colitis.

The significance of such a colitis is, I believe, infection, which may be the result of stasis or, as has been argued by some authorities, among them Keith, of London, the infection being the cause of the stasis, resulting in injury to the intestinal musculature.

The effects of stasis and its resulting toxemia are numerous and manifold.

Much work has been done on the excretion of indican and the ethereal sulphates, and there is no doubt that an excess of indican is often associated with serious intestinal disturbances. But many persons pass large amounts of indican for years and remain in good health, and, on the other hand, indican is not passed in many instances in which the patients might be thought to have alimentary toxemia.

It is generally allowed that the poison is not indol, indican, or ethereal sulphates, but just as we do not know what is the poison in uremia or diabetic coma, so we do not know certainly which are, in every case, the offending microörganisms; nor do we understand the circumstances favoring their appearance and development.

Herter taught that there are probably three groups of cases:

(*a*) The indolic, in which the probable fault was that of the colon bacillus invading the lower part of the small intestine and the patient was unable to digest carbohydrates and usually passed an abundance of indican.

(*b*) The saccharobutyric, in which the organism mostly concerned is the Bacillus aërogenous capsulatus; the abnormal changes here occur in the large intestine.

(*c*) A third group composed of groups (*a*) and (*b*).

The investigations of Mutch, of London, "on the bacterial activity of the alimentary tract," have revealed the following facts:

1. The infection of the ileum with coliform organisms is uninfluenced by the gastric secretion.

2. The excretion of the complex tyrosin and tryptophane decomposition products varies directly with the degree of that infection with coliform organisms.

3. The excretion of indoxyl, indolacetic acid, and hydroxyphenylacetic acid is uninfluenced by an infection of the ileum with streptococci or with Bacillus acidophilus of Moro, and that hydroxyphenylacetic acid varies in proportion to the degree of ilial stasis.

4. That an infection of the ileum with Bacillus aminophilus occurs in constipated persons with subnormal blood-pressure, but not in other constipated patients.

Chronic infection of the ileum with Staphylococcus citreus has been shown to be present with chronic septicemia due to the same organism and with the chronic joint, lymphatic, and splenic changes classified as Still's disease.

The constitutional changes and those in the joints, lymphatic glands, and spleen were abolished by colectomy.

Fifty-five ilea of patients without Still's disease were free from Staphylococcus citreus.

The above is a brief citation of a portion of the exceedingly interesting work Mutch is doing relative to intestinal chemistry and bacteriology.

The fact remains, however, that whether we have been able to isolate the poison or poisons, or whether such a poison is the result of putrefactive decomposition of stagnant food material, or the result of direct infection of the intestinal tract itself, there has already accumulated a large amount of corroborative evidence to substantiate the fact that under improved intestinal drainage an amelioration or cure takes place in many or all of the symptoms of intestinal toxemia.

It has been constantly argued that thousands of persons are constipated and yet do not suffer from symptoms of poisoning.

When we recall the physiology of the colon it is borne in mind that food enters the cecum through the ileocecal value in practically a fluid consistency, and that during its passage along the ascending and the first half of the transverse colon the fluids are absorbed, leaving the fecal residue, and that from the distal half of the transverse colon onward there is but comparatively little absorption.

I think it is well substantiated clinically that when the arrest occurs in the descending colon, sigmoid, and rectum it is accompanied by little or no symptoms of poisoning.

I have recently had a patient who suffered from a profound constipation due to adhesions involving the upper portion of the sigmoid; her bowels did not move for periods of four or five days, and then unsatisfactorily after repeated enemata, yet she did not suffer from any symptoms which could be attributed to toxemia. The blood showed, in moderation, the changes generally attributed to constipation, namely, leukopenia, mild anemia, and relative lymphocytosis, but otherwise her general health was comparatively good.

On the other hand, stasis of the cecum and ascending colon is not infrequent with toxic symptoms.

Nature has established certain protective agencies or lines of defence which under physiological conditions prevent the entrance of toxins into the circulation. These are:

1. The healthy intestinal mucous membrane which presents a barrier by its relative impermeability so that their diffusion takes place slowly and time is allowed for the action of the digestive secretions which destroy the microbes and neutralize the poisons.

2. The gastric and pancreatic juices and, to a less degree the bile, all have destructive and neutralizing properties.

3. The liver, which has a high degree of detoxinizing power.

4. The glands of internal secretion.

In undertaking the treatment of any case of constipation the physician must constantly bear in mind that it is a condition into which many factors enter, both psychic and reflex.

There are numerous cases on record which have been treated successfully by the mental healers and the Christian Scientists. Fear, whether conscious or subconscious, is undoubtedly an underlying factor—fear that the bowels will not move. Often a firm assurance that they will move and a discontinuance of the nightly pill are all that is necessary to accomplish the results.

In the past two years we have had a not inconsiderable number of patients who have been treated, so to speak, by "assurance," with good results.

Of course, in all cases of constipation the education of regular habits in going to the toilet and in not being hurried or interrupted are of the greatest importance.

It is a matter of common experience that exercise is most beneficial to intestinal peristalsis; this is due to both the increase of food intake with its resulting residue and the creating of rapid changes in intra-abdominal pressure, thus, so to speak, massaging the intestines and producing more active peristalsis.

Among the patients who are unable to obtain active outdoor exercise a daily routine of calisthenics may be prescribed. Much help will be found in a practical, well-illustrated monograph by Muller, entitled *My System*.

Massage is of benefit in certain selected cases in which a general state of intestinal inactivity exists, but should not be employed as a routine measure. It should be practised by one who has some knowledge of the general anatomical conditions. Its prolonged or injudicious use may lead to conditions of spasm, and may ultimately prove more detrimental than beneficial. It is contraindicated in spastic conditions of the colon or when there is any suspicion of appendix disease.

Poorly nourished individuals with the enteroptotic habitus and visceral ptosis, who are almost invariably constipated, require two essentials: the first is an improvement in their general condition and the second a good, firm, well-fitting abdominal support. In these extreme cases of malnutrition nothing short of a thorough rest cure will help their general condition.

Such a rest cure consists of from four to five weeks in bed with

forced feedings, giving them food of high caloric value in small quantities six times a day. The rest in bed removes the drag from the mesentery and allows a straightening out of any tendency to angulation in the intestines.

Fat is first formed in the great omentum, where the blood supply is richest, and such an increase in the omental fat serves as a padding to the prolapsed viscera, giving them a very material support.

By such a "cure" from ten to twenty pounds' weight can be added. Then on allowing them to resume the upright posture—a process which should always be done gradually—a firm, well-fitting support is furnished, which should be adjusted in the morning before getting up and worn through the day. Such a support should be either in the form of a belt or corset. Not only do these supports tend to raise the viscera into a more normal position, but they increase the resistance of the abdominal wall. This resistance is important in raising the intra-abdominal pressure in the act of defecation.

We have had many cases of apparently hopeless invalidism restored to an active, useful life by such procedure.

Diet is an all-important factor in every case of stasis, not alone the character of the food, but the quantity. Some persons, especially those with gastric indigestion, either do not eat enough or else select such articles as leave insufficient residue to stimulate intestinal peristalsis.

To a large degree intestinal activity depends upon the mechanical stimulation of the cellular food residue and the distention of the bowel by food. This distention in its turn is due to the indigestibility of the cellular elements, so that diets lacking in the cellular residue materially diminish peristaltic action.

The chief chemical stimulants of intestinal activity are sugar, organic acids, and their salts. To a less degree are the neutral fats, soaps, and glycerin representing the digestion and bacterial decomposition of meats.

Some authors, among them von Noorden, maintain that the coarse, scratchy diets are suitable in practically all cases of intestinal stasis, even in the presence of mucous or mucomembranous colitis; and that by persisting in them the bowels ultimately become regular and the colitis is cured. Such diets contain practically all the vegetables which are all more or less rich in their cellular elements; especially to be mentioned are oatmeal, whole wheat (not brown) bread, and such fruits as prunes, apricots, etc.

However, when there is a colitis, as evidenced by the presence of mucus in the stools, or when abdominal palpitation shows spasm of the colon, our experience has been that such cases do better on a less scratchy and irritating diet, using such articles as leave less residue, and having them prepared largely in the form of purées.

As the colitis and spasm improve the coarser articles of diet may be gradually added.

The medical treatment of intestinal toxemia is practically purely dietetic, for in no case have we seen more than temporary improvement from the so-called intestinal antiseptics. In certain instances apparently gratifying results are experienced by the lactic acid producing bacilli, but on the discontinuance of their use the old train of symptoms soon recur.

In cases of toxemia one will find the dietetic suggestions of Combes to contain much valuable data. We have used his work largely as a basis for our treatment in auto-intoxication, with good results.

The aim in every case of stasis is to restore the bowel to its normal function, to cut out the use of cathartics, and to correct a faulty hygiene and adopt a diet suitable to the individual case, employing such mechanical measures as are indicated.

There is one preparation, however, which must be considered in relation to these conditions, namely, paraffin oil. The use of this oil was called to the attention of the profession by Lane, of London, and it has deservedly acquired a wide reputation.

There are many cases of stasis in which the circumstances in life prevent carrying out many of the above-mentioned details, where certain anatomical conditions exist that require more aid than we can give by means of diet, supporting belts, and accessories, and yet when we do not feel that the condition is such that an operation is imperative. Paraffin oil, in a large number of these cases, gives most excellent results and, so far as we know, may be used indefinitely and in large amounts. Its results are particularly gratifying in the dry or rectal types of stasis. Some writers have laid stress on the use of a more viscous oil, namely, those of the highest specific gravity; but in our experience this has not been a very important point and the lighter oils have given equally good results.

Some patients complain that the oil oozes from the anus or will be passed without producing any movement. This can sometimes be avoided by the use of a little agar-agar in conjunction with it. As a rule, after a few days and when the fecal stream has been started the leaking ceases. Agar-agar is a simple carbohydrate from seaweed. It has the property of absorbing water and resists the action of intestinal enzymes and bacteria; it passes practically unaltered through the intestines, increasing the intestinal residue, but in itself is not particularly efficacious. It should not be used in cases in which there is any evidence of an inflamed intestinal mucous membrane.

In the majority of cases of beginning treatment for stasis it will be found necessary at first to move the bowels every second or third day either by the use of saline or oil enemata. Such a course

of enemata will in itself clear out an impacted rectum and often start the bowels working in a normal manner.

No paper on the subject of stasis and intestinal toxemia is complete without the mention of autogenous vaccines. Within the past two or three years some sporadic work has been done along these lines with varying degrees of success; for the past two years we have been using such vaccines, having cultures made from the stool and taking out the predominating organism, which generally consists of the colon bacilli.

In many instances vaccines used in conjunction with diets and general hygienic measures have given us most excellent results, the symptoms of toxemia clearing up; and in some cases the bowels have taken on a normal function with little or no further treatment. We feel that in the more pronounced cases of toxemia they are certainly worthy of a trial.

Organotherapy, although still in an empirical stage, infrequently gives some brilliant results in stimulating the insufficient antitoxic function of the organs of internal secretion. Thyroid extract administered in grain doses after meals in many cases of long-standing toxemia helps the overworked internal secretions in their efforts to neutralize the poison.

Our endeavor has been, in a limited time, to make a brief outline sketch of the present-day conception of stasis and its medical treatment, together with its complication, intestinal toxemia.

The surgical aspect of the subject will be discussed by Dr. McWilliams.

Surgical Considerations by Dr. McWilliams.

The surgical treatment of constipation and intestinal stasis is probably the most frequent and prominent topic before the medical world today. Scarcely a medical journal appears without an essay on intestinal stasis. Notwithstanding the discussion and experimentation that is being conducted, the proper surgical treatment of the condition will eventually be worked out on a rational basis, and it will find its proper place as other procedure in surgery have done in the past. In the mild and non-toxic cases, it cannot be too strongly emphasized that thorough medical measures should be persistently conducted before thinking of resorting to surgery. In the severer toxic cases it is well to have a thorough Roentgen-ray examination of the intestinal tract made at the outset of the treatment, so as to rule out the presence of any gross surgical lesion in order that valuable time may not be lost in unavailing medical treatment when the patient may need surgery. Surgery is a valuable succedaneum to medical treatment when it is used with intelligence and judgment. We take issue with those who advocate the removal of the large bowel for two

main reasons: (1) because of the immediate high mortality of the operation, which is between 30 and 40 per cent., an altogether too great mortality, it seems to us, to warrant the surgeon in performing it for a malady which, in the vast majority of cases, is not in itself fatal, and (2) because the removal of the entire large bowel is at times followed by an intractable and exhausting diarrhea which may last for months. At the present time the writers know of a patient whose entire colon was removed for intestinal stasis three months ago in one of our large institutions. Her condition has been and is now most pathetic, for she has been in bed since the operation, having from twenty-five to thirty loose stools a day, and these cannot be controlled. Lane says these cases of diarrhea after operation will eventually clear up; but what opprobrium is brought upon surgery when an operation is done which may lead to such an unfortunate result—worse than the lesion for which the operation was performed.

The short-circuiting operations, such as placing the terminal ileum in the sigmoid flexure or rectum, have a low mortality, but, as a rule, they have failed to cure because of a backing up of the feces into the excluded gut, where they remain, allowing absorption to take place from them. Distressing diarrhea may also occur after this operation. The operation has, however, seemed to do good in some selected cases, and may be tried, but the surgeon should not be disappointed in not effecting a cure. It would seem as though this operation could do the patient no great harm other than a more or less transitory diarrhea.

An operative procedure which, we believe, will be found to be the best in those severe cases in which no other surgical lesion can be discovered to account for the stasis, is the removal of the cecum, ascending colon, hepatic flexure, and half of the transverse colon. In this operation the immediate mortality is lower than in total colectomy, and the remaining portion of the large bowel will allow of a solidification of the feces, so that there will be no subsequent diarrhea, or if there be any, it will be but slight and transitory. The ends of the ileum and the transverse colon may be closed and a side-to-side anastomosis made between them, or if speed be advisable a Murphy button may be placed between the end of the ileum and the side of the transverse colon, the end of the colon being previously closed.

Before resorting to this radical procedure, however, a thorough exploration should be performed to endeavor to find some surgical lesion which may be removed by less severe measures. A right rectus incision should be made, beginning at the navel and running up as far as necessary. The incision is made close to the inner border of the rectus muscle, which is retracted outward. The gallbladder is first explored for calculi and for adhesions to the duodenum and transverse colon. Our feeling is that if it can be done

without undue risk to the patient the gall-bladder, if it is adherent or is pathological, should be removed, as this will be the best guarantee against a recurrence of the adhesions and inflammation. Gastric and duodenal ulcers should be next searched for and, in the ordinary case, if they be present all that will be necessary will be a gastro-enterostomy, to which may possibly be added the closure of the pylorus by wrapping around it a strip of fascia, best taken from the rectus aponeurosis.

The various mechanical causes of intestinal stasis should then be searched for and, in order to understand exactly what we are to search for, it will be necessary to give a brief *résumé* of these causes. It is only when the contents of the large intestine stagnate unduly that harm results, and the more the stagnation in the large intestine, the greater is the resultant harm. The worst cases are those in which prolonged stasis occurs both in the large and in the small intestine. Stasis in the lower end of the ileum is produced in three ways: First, the simplest of these is for the appendix to be so placed that it interferes with the passage of the ileal contents into the cecum when the patient is upright. The appendix is then usually internal, retrocecal, and its tip firmly attached high up, allowing the proximal and distal loops to sag, while the portion of the bowel attached to the appendix remains fixed, producing obstruction. A second means of obstruction is the following: any marked degree of stasis in the large intestine will lead to delay in the passage of the ileal contents into the cecum, which is already overfilled. The loaded ileal coils consequently drop into the pelvis and the terminal coil of the ileum rises vertically over the pelvic brim to the ileocecal entrance, and the ileal contents are therefore compelled to ascend a long vertical path, the prominence formed by the pelvic brim and the sacral promontory producing more or less obstruction. In some patients the cecum also occupies the pelvis, and it may become abnormally elongated, dilated, and mobile. A third way in which ileal stasis is produced is by Lane's ileal band, which is caused by the continued pull on the mesentery by the overloaded ileum, resulting in the formation of thickened bands in the situations where the pull is the greatest. These bands tend to prevent the dropping of the ileal coils; that is, some of the coils drop while others remain fixed. In general enteroptosis, if all the coils prolapse equally there may be no difficulty in defecation. It is the irregularity in the position of the prolapse which in other cases produces the difficulty. A single band, Lane's ileal band, placed within four inches of the end of the ileum is most potent to produce obstruction in the subjects with ileal stasis. With this band, while the patients are recumbent, no obstruction exists. This is the reason why recumbency in bed, the importance of which Dr. Barclay has dwelt upon, is so helpful. In the upright posture, however, the cecum drops on one side of the fixed band

while the ileum prolapses on the other side. The bowel is consequently held up at the kink and its lumen is obstructed at this point. The results of these three methods of producing obstruction are the same. Bacteria invade the stagnant ileum from the cecum and ascend the small intestine, where their influence is exerted the most severely at the upper end, as on the duodenum, causing ulcers; on the gall-bladder, producing inflammations and calculi; and on the pancreas, causing chronic pancreatitis. Jordan says that in operations on the subjects of ileal stasis the duodenum, which is fixed, is always found to be distended, due to the kink producing obstruction at the junction of the fixed duodenum with the free jejunum, produced by the jejunum being pulled vertically downward by the overloaded lower ileal coils.

Stasis in the Large Bowel. The cecum tends to become dilated, elongated, and displaced into the true pelvis, which it occupies to the inconvenience of other structures. This tendency to fall is met by new bands being formed, external to the cecum and ascending colon, which fix these structures to the abdominal wall (Jackson's membrane). The lowest band includes the appendix and may produce symptoms of varying severity comprised under the term of "chronic appendicitis." The next kinks which develop are those at the hepatic and splenic flexures. These are very rare. To meet the drag caused by the prolapsed transverse colon in addition to the loaded cecum, peritoneal bands develop which drag these flexures upward and convert the passage from a round turn into a sharp kink. This is exaggerated still further by the formation of bands connecting the adjacent surfaces of the prolapsed transverse colon with the sides of the ascending and descending colons, which serve to transmit some of the weight of the loaded transverse colon through the ascending and descending colons to the abdominal wall, thus taking off some of the strain from the convexity of the stomach. These bands are evolutionary and are not inflammatory. The transverse colon may sag so like a V that its apex may come to occupy the pelvis, where it may become adherent.

By the kinking at the hepatic and splenic flexures, obstruction may rarely be produced. A kink may develop at the level of the iliac crest on the right side, where a strong band of adhesions may attach and control the lumen of the ascending colon sufficiently to cause some obstruction at this point. Another band may develop between the under surface of the liver and gall-bladder and the pylorus and transverse colon, producing obstruction. The "last kink" affects the large bowel on the left side where it crosses the brim of the true pelvis. These latter bands develop early in life and form between the peritoneum of the iliac fossa and the outer surface of the mesentery. The ovary and Fallopian tube are often involved in these adhesions.

We will now continue the exploration of the abdomen, which was interrupted above. Adhesions binding the transverse colon and pylorus to the liver and gall-bladder should be divided transversely. The operative treatment of duodenal distention, due to kinking at the duodenojejunal junction, resolves itself into the removal of the obstruction at the lower end of the ileus, and consists in the transverse division of the controlling band, *i. e.*, Lane's ileal band, with vertical suture of it and in the removal of the appendix. An elongated, dilated, mobile, prolapsed cecum may be latterly plicated after removal of the appendix. That is, two of the vertical striæ are sutured transversely together by a continuous silk suture, or even more of the diameter than this may be infolded, and the cecum may then finally be sewed fast to the iliac fossa, "Jackson's membrane," binding the outside of the cecum to the abdominal wall, should be divided and sutured. A long, V-shaped, transverse colon, which is adherent in the pelvis, should be freed and lifted up. Adhesions binding its sides to ascending and descending colons should be divided and the transverse colon may be secured in its place, if thought advisable, by Coffey's suspensory operation. In this procedure the gastrocolic omentum is sutured widely to the anterior abdominal wall. This not only supports the ptosed transverse colon, but also the stomach, or, what is perhaps better, the great omentum below the transverse colon, with the gastrocolic omentum above, the transverse colon may together be sutured to the anterior abdominal wall. This elevation of the transverse colon will do away with any possible kinking at the hepatic and splenic flexures. Any band kinking the sigmoid should be divided.

Such in brief outline are the surgical procedures which may be done in cases of intestinal stasis when surgery is needed. We may say, however, in conclusion, that in the majority of cases, provided there be no congenital defect present, the conditions producing intestinal stasis are preventable and should not be allowed to develop into the stage where operative intervention is necessary. A more intelligent appreciation of the importance of exercise, diet, proper hygiene, of the position of the viscera, and of adequate support of the abdominal organs will go a long way toward preventing the stasis of large amounts of material at given points in the intestine. With this accomplished the development of chronic intestinal stasis will be forestalled. If after prolonged study by a competent medical man who has a proper appreciation of the physiology of the abdominal organs, supported by good Roentgen-ray pictures, it seems wisest to operate, in the event of failure of thorough medical treatment, the great question confronting the surgeon is to know what surgical principles to carry out and how much to do. The one thing which surgeons seem agreed upon that is proper and allowable to do is this, namely, to divide any adventitious bands,

which the Roentgen-ray pictures indicate are causing obstruction, and to remove the appendix. Further procedures bring the surgeon upon debatable ground. Opinions and statistics differ so upon the value of the various visceral supporting operations that a conservative surgeon with our present knowledge will hesitate before adopting most of them. Except in very exceptional cases the short-circuiting procedures should be avoided, while the removal of the whole large intestine, in our opinion, should never be done for intestinal stasis alone. In the severest and worst cases a safer operation is the removal of the cecum, ascending colon, hepatic flexure, and half of the transverse colon. In any case, both before and after any operative procedure, a well-fitting, efficient, supporting apparatus should be worn and medical measures persisted in, particularly the use of Russian oil in gradually decreasing doses. Wilson[1] says: "It is interesting to observe Lund's[2] convincing conclusions that cures will be rare after operation for visceroptosis. The adverse reports that are rapidly accumulating are convincing that visceroptosis is not always cured by operation and that there must arise some skepticism when an overenthusiastic operator reports brilliant results that no one else can see or obtain."

This paper has not dwelt upon infections of the large bowel, but when this is present, resisting all medical treatment, a better procedure, and one more efficacious than an appendicostomy is an ileostomy or opening in the lowest portion of the small intestine, which will assure absolute rest for the bowel below the opening.

THE WASSERMANN REACTION IN PREGNANCY.[1]

By Albert M. Judd, M.D., F.A.C.S.,

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The serum diagnosis of syphilis has in no department of practice proved of more value than in that of obstetrics, involving, as it may, two patients at the same time. Further, the routine examination of all antepartums for the Wassermann test, wherever possible, is strongly urged as latent syphilis may be shown in no other way.

[1] Med. Rec., April 17, 1915, p. 775.

[2] The Surgeon and the Ptosis Problem.

[1] This paper was read before the Hospital Graduates' Club of Brooklyn at a stated meeting, and the Plainfield Clinical Society. A few additions have been made to the paper since that time, consisting of a larger number of examinations, but our conclusions have been practically the same.

For some time this has been carried out at the Kings County Hospital, and, more recently, at the writer's suggestion, the routine examination of fetal serum as obtained from the severed umbilical cord at birth, both procedures with the happiest though not always conclusive results. We have still to learn much concerning the Wassermann reaction, especially from the standpoint of treatment, dosage, pregnancy, time of administration, contra-indications, etc.

The percentage of positive reactions varies with the period of the disease, and whether the infection is acute or latent, hence primary cases where the lesion is present less than two weeks usually show negative, while if the sore is present over four weeks, 75 per cent. positive is found. Secondary syphilis, with symptoms, gives positive in 90 per cent. and tertiary in 75 per cent. Syphilis without symptoms (latent) shows in the untreated cases, 75 per cent. in early cases, and about the same (76 per cent.) in the late ones. The few other diseases showing positive Wassermanns are not likely to be confused with syphilis, or can be readily excluded, such as pneumonia, which is said to give positive for a few days following the crisis; malaria giving 20 per cent. positive in cases with fever and untreated; the tubercular type of leprosy showing positive in a large percentage of cases; and yaws, which gives as high a proportion of positive as syphilis.

The test was made 892 times in our wards, of which 821 were negative and 71 were positive (7.9 per cent.). A considerable number, not included, were admitted in labor and the blood not examined, though we are now having these taken as well, postpartum. A majority of the positive patients examined had no visible lesions, and would have been overlooked but for the routine Wassermann.

The treatment varied from "606" to mercury by inunction and hypodermics. Those who received no treatment before delivery either refused it or were admitted in labor, and one case was overlooked inadvertently. Those admitted in labor whose Wassermanns were positive postpartum received treatment before discharge in the majority of cases. We are not as yet able to control the treatment of syphilis in pregnant women when they are admitted to the hospital for some cause other than pregnancy, but we expect eventually to do so, at which time every pregnant woman with syphilis, whatever the period of gestation and in the absence of contra-indications in the kidneys and eyes, will receive "606." We do not share the fear expressed by some of giving "606" in late pregnancy.

One case admitted in labor had been given salicylate of mercury by hypodermic injection intermittently before admission, with no effect on the lesions, and she presented some beautiful specimens of rupia in addition to a 4+ Wassermann; the child was saved, however, by the treatment and had a negative blood report, though

a rash developing a few days later was pronounced probably specific by the dermatologists. Of the living children (277 examinations) all were born without lesions and but 12 of the 277 had a positive Wassermann. A few were not examined for this reaction, as that was not a part of the routine at the time of their birth.

One of the babes with a minus Wassermann was admitted to the Children's Hospital a few months later in a moribund state with a diagnosis of marasmus. Examination of the blood and spinal fluid proved a 4+ Wassermann.

Another woman had a very interesting history: Her first blood examination was 4+ on April 10, 1913; "606" given April 27; 4+ on May 15, 1913; "606" given May 27, and June 19, 1913, and no further treatment given. Later examination, on October 16, was 4+, and she delivered a dead and macerated fetus on October 28, 1913.

The history of miscarriages was of doubtful value, a majority of the positive cases recording that accident one or more times, while the remainder were either primigravida or had borne living children, with no miscarriages. Few of the series of miscarriages had histories pointing definitely to syphilis as a cause. One had a live child four and a half years ago, alive and well today; then occurred four premature labors, all at or about the seventh month, for the last of which she entered our service in labor in March, 1913, following which she has had a 4+ Wassermann. She left without treatment. Seen some time afterward she was again pregnant, had reached the sixth month with a live child, and her blood was still 4+ without any treatment. She entered our service at once for treatment and the outcome was awaited with interest. This patient received numerous injections of mercury salicylate, both before and after entrance to the hospital, none of which was given until after the sixth month. While they did not affect her reaction, being 4+ at the time of delivery, she delivered herself of a live child, weighing 9 pounds 10 ounces, without visible lesions and with a negative Wassermann. This child, however, became ill at the end of one month, was admitted to the children's service of the Kings County Hospital as a syphilitic, and died of syphilis at the end of the third month.

Another case had a live child in 1909 which died at the fifth week, she states, of an infected cord, one miscarriage at the fifth month in 1910, and another at the third month in 1911. She had a live child in October, 1913, without any treatment, but the child's blood showed a 4+ Wassermann at birth, and it developed a rash a few days after birth, which, while the dermatologists were unwilling to call it syphilitic, cleared up after mercury was placed under the baby's binder. The mother's Wassermann varied from a very doubtful positive on the first examination to three decided negatives on subsequent tests.

Baily, quoting Bat and Daunay, considers that a solitary negative in pregnancy does not mean surely that syphilis is absent, but one positive is evidence of certain maternal and probable fetal infection, and indicates the necessity of active treatment. They find when infection has occurred sometime after conception there is a higher percentage of positive results with the mother than with the infant.

Treatment of the mother during pregnancy gives a negative reaction in the infant, but one negative does not necessarily mean that the infant is all right and can be suckled by a healthy wet-nurse, as syphilis may be latent. Of 35 mothers whose babes showed signs of syphilis, 26 gave a positive and 9 a negative reaction. The large majority of cases with positive at birth, later develop symptoms of syphilis, and the large majority of cases negative at birth remain healthy.

Examination of the maternal blood shows:

1. The mother may be positive and the child minus. (A majority of our cases were such.)
2. The mother may be minus and the child positive. (A few of ours agreed.)
3. The mother may be positive and the child positive. (Ours agreed only in untreated cases.)
4. The mother may be minus and the child minus. (As would be expected, there our records coincide.)
5. The mother may be doubtful and the child positive. (We now have such a case under observation.)

Probably one need have little fear for the child if the mother is negative. Of congenital syphilis it may be said that practically all infants or children showing symptoms give positive reactions, but not all children born of syphilitic mothers; while of living children born of syphilitic mothers nearly 50 per cent. give a negative. Our percentage for such cases was even higher, owing to the mother having had treatment.

The precaution must be observed, however, that if the child has been delivered after an anesthetic has been given to the mother the blood of either the mother or child be not examined for a full twenty-four hours after delivery, as the results may be erroneous. The same holds true regarding the ingestion of alcohol by the mother.

Boas examined the reaction in 44 infants, who showed either syphilitic lesions or were born of syphilitic mothers, and his results were: 20 positive and 24 negative. 20 positive: 16 had symptoms at birth or within three months, 4 had no symptoms in three months, and the reaction became negative rapidly. 24 minus: 17 remained negative and had no symptoms; 5 developed symptoms and positive reactions; 2 died with negative and yet proved to be syphilis.

Antisyphilitic treatment during pregnancy can result in the birth of healthy children and such children are free from syphilis and may be quite healthy or show various positive defects. Latent syphilis

(positive reaction without symptoms) is common in early years, explaining Profeta's law, immunity of the healthy children of specific mothers. The immunity of the child in Profeta's law and of the mother in Colles's law is only apparent; they cannot contract the disease because they already have it in latent form.

Miller[2] states: "The Wassermann has been positive in practically all forms of congenital malformations." In addition there should be included the cases of so-called marasmus, more properly infantile atrophy.

One of the most marked tendencies of babies born of mothers late in the maternal disease is that to hemorrhage and jaundice. We use whole blood in these cases in our service at the Kings County Hospital with great success.

An intermittent fever in the later months of pregnancy has been pointed out by Taussig,[3] of St. Louis, as being often of syphilitic origin.

The further development of luetin by Noguchi will place in the hands of the general practitioner a method of diagnosis easily used by himself and within reach of the ordinary patient's purse. We must realize that the fee for caring for obstetric cases is so small that the practitioner cannot afford to have any portion of it taken away from him by the laboratory man.

The treatment of syphilis during pregnancy is the same as at any other time.

The author differs in his opinion from those who state that the existence of a pregnancy is a contra-indication to the use of salvarsan and adopts the attitude of von Zeisl, who states that because of the rapidity of its action, it seems especially suited to syphilitic pregnant women with a view to the prevention of abortion and the delivery of a sound child.

I wish to thank my associate, Dr. William Pfeiffer, for his assistance in compiling these records.

THE CRANIAL DEFORMITY OF OXYCEPHALY; ITS OPERATIVE TREATMENT, WITH A REPORT OF CASES.

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During recent years, much interest has been aroused in the relation of cranial deformities to optic nerve atrophy; Patry has stated that almost all cranial deformities occurring in the

[2] Cleveland Med. Jour., July, 1912.
[3] Surg., Gynec. and Obst., July, 1910.

first five years of life result in optic nerve atrophy. In 1873 Michel was the first to observe the frequency of optic nerve atrophy in cases of cranial deformity, and this is especially true of those cases of cranial deformity known as the "turmschädel" variety—meaning merely tall heads or high skulls; this is particularly true of the extreme type of the turmschädel skull—the oxycephalic type which is not merely a tall head but one with a prominence or protrusion at the anterior fontanelle.

NAMES. Much confusion has arisen in the literature of this subject due to the variety of names that have been used to designate this cranial malformation; among those names frequently observed are "turritum caput" (Welker); "tete a la thersite" (Hamy); "acrocephalie" (Lucæ); "spitzkopf" and "hypsicephaly" (Oliver). These names are used in describing abnormally tall heads whether of the frontal or occipital type. The two names which have been used most frequently and interchangably are turmschädel and oxycephaly, and it seems wiser to consider the two names as applying to one condition which differs only in the degree of the deformity, "turmschädel" or "steeple-shaped skull" for the mild form of the condition, where there is no definite prominence or protrusion at the anterior fontanelle, and "oxycephaly" for the more severe cases with a prominence at the anterior fontanelle.

Most of the observations of this condition have been made by oculists, since the patients have been brought to them on account of the failing eyesight and nystagmus; very frequently the cranial deformity has been overlooked. Von Graefe reported the first case in 1866 in a male child, eight years of age, whose head was very high but narrow transversely; there had been a gradual onset of blindness which proved upon ophthalmoscopic examination to be due to a "symmetrische neuroretinitis"—the picture of a typical choked disk. This case apparently was one of mild degree—the turmschädel type. Since then many cases have been reported—about 80 in all—the vast majority of which have been of the turmschädel type, merely tall heads with optic nerve atrophy of varying degrees; unless there is visual impairment, the cranial deformity is rarely considered important enough to warrant a doctor's opinion and therefore very few such cases have been carefully examined; such cranial deformities however, must be very mild, for slight cranial malformations, especially of the turmschädel variety, do produce ocular disturbances in varying degrees—the greater the deformity, the greater the eye disturbance. Hanotte has stated that practically all of the so-called "oxycephalic" heads in the "Ecole d'Anthropologie" (Catacombs), and in the "Gallerie d 'Anthropologie du Museum" are merely tall heads with no protrusion at bregma, being similar to the skull of Sir Walter Scott. However, if eye disturbances were produced by such tall heads, they should undoubtedly be classified as mild types of the turmschädel

variety of cranial deformities. Not more than 20 typical cases of oxycephaly have been reported, that is, cases of the severe turmschädel variety of cranial deformity with a prominence or protrusion at the anterior fontanelle; all of these cases produced optic atrophy of varying degrees.

ETIOLOGY. Many theories have been formed to account both for the cranial deformity and its closely related optic atrophy. Most observers are now agreed that a premature synostosis of the occipital, parietal and the temporal bones has allowed the brain to grow and expand only in the direction of the anterior part of the skull, producing either the high turmschädel type of skull, or in severe cases and more rarely the enlargement and bulging prominence at the anterior fontanelle of the oxycephalic skulls; the resulting increase in the intracranial pressure gradually producing a secondary optic atrophy, very similar to the effect of a brain tumor, which as it grows, slowly raises the intracranial pressure and so produces a typical choked disk, and if prolonged, a secondary optic atrophy. It was formerly believed, especially by Manz, Ponfick and others, that a narrowing of the optic foramina was caused by an osteitis, forming hyperostoses which compressed the optic nerve and in this way a primary atrophy resulted, as well as the other cranial deformities; such a view, however, has not been confirmed by autopsies by Vortisch, Weiss, and Brugger except in 1 case reported by Ponfick and 1 by Michel.

Bertolotti firmly believes that rachitic craniotabes and oxycephaly belong to the same rachitic process, and only after the synostosis of the sutures of the skull does the picture change and oxycephaly individualize itself. But what is the exciting cause for the premature synostosis of the sutures of the skull? Very many opposing views are held; Virchow, Vortisch, Hirschberg, and others believe that the premature synostosis is due to a fetal hyperemia and inflammation of the meninges due to inherited syphilis, nervous instability from alcohol, epilepsy, and the result of difficult labors. Bertolotti, Meltzer, Obermuth and others are convinced that the underlying cause is rickets—as Bertolotti says, it is a "dystrophy of rachitic origin," whereby mild meningitis causes a slight inflammation of the sutures of the skull and hence stimulates the genetic growth of these bones; in this manner the sutures become closed prematurely, especially in the posterior portion of the skull, and as the gradually increasing intracranial pressure can only expand in the anterior part of the skull, the deformity of turmschädel and oxycephaly results. Bertolotti states that in 85 per cent. of his cases there are skeletal evidences of rickets; the report by Meltzer in his review of 20 cases is the same.

Such, however, is not the view of many other observers, such as Fletcher, Enslin, Dorfman and others, who believe that the condition is due to some underlying cause the nature of which at

present remains obscure; it is not believed to result from an early meningitis in that the cranial nerves are not affected, nor is there a marked mental defect; in fact, the cases are all unusually bright and intelligent; nor have there been any cases reported which at autopsy disclosed a hydrocephalus or even any signs of a previous meningitis. The theory of its being a "dystrophy of rachitic origin" is very strongly opposed by the fact that in cases suffering from rickets the closure of the sutures is delayed (not premature) and the deformity of the head is different; besides, few cases have been reported which have disclosed definite skeletal signs of rickets, such as enlarged radial epiphyses, rosary, etc.; Oberwarth however, states that 5 of his 7 cases showed definite signs of the "Englishe-krankheit." In the 4 cases reported here no such signs were to be found, nor were they to be found in any of the cases reported by Enslin, Carpenter, Hirschberg, Stephenson, Fletcher, Dorfman, Dodd and McMullen and others.

There seems to be no predisposing factor in producing this condition. No race is exempt apparently; about an equal number of blondes and brunettes have been reported. It is far more common in males than in females, the proportion being about 5 to 1; of 17 cases of turmschädel reported up to 1893, 15 were males and only 2 were females (Friedenwald). Of the 7 cases each of Videcky and Hirschberg, 6 were males; of the 8 cases of Oberwarth, 6 were males. Heredity has little or no effect, the family history usually being very good and the other children of the family being in excellent health. Hirschberg reports 1 case where the maternal grandfather was an oxycephalic; Weiss and Brugger mention 2 oxycephalic brothers seen by Oeller, and Hanotte states that Hamy observed 2 oxycephalic sisters; Carpenter also reports the cases of 2 oxycephalic sisters. Apparently syphilis is not a factor, nor is traumatism.

The intelligence is unimpaired, the patients being unusually bright and intelligent. If mentally backward it is usually due to loss of eyesight, *i. e.*, "deprivation" (Ireland), or to the gradual deterioration of epilepsy. Practically all of the cases of Meltzer, Groenouw, Fletcher, Enslin, Friedenwald, Hirschberg, and Oberwarth have been normal mentally.

Among the possible mild types of turmschädel, such as abnormally tall heads, Patry cites the examples of the skulls of Sir Walter Scott, Paracelus, William Humboldt, Mechel and others who were exceptionally intelligent men.

COURSE. There are three main groups of turmschädel cases classified by Fletcher according to the date of the onset.

1. When the cranial deformity with possible optic atrophy was present at birth—the congenital cases; these are comparatively few in number.

2. When the cranial deformity and possibly "large eyes" are

observed during the early months of life or during the first two years; this deformity and impairment of vision are gradually increased.

3. When the earliest signs are noticeable for the first time between the second and sixth years of life, usually some visual impairment, associated with headaches and occasionally with "fits." This group includes the majority of cases, and it has frequently been observed that the cranial deformity becomes much worse and the headaches and "fits" more severe as the impairment of vision progresses and the resulting blindness occurs. The duration of life is not shortened in many mild cases, though it is very exceptional to hear of cases after fifty years of age; Hirschberg and Grunmach believe that very few cases of average severity survive puberty.

Regarding turmschädel as the mild form of oxycephaly, both being due to the same cause with only a difference in the degree of severity, let us consider then its characteristics, remembering that in oxycephalic cases there is a bony prominence at the site of the anterior fontanelle.

SIGNS. There are really three cardinal signs of the trumschädel type of cranial deformity, namely:

1. The type of cranial deformity.
2. Exophthalmos with divergent strabismus.
3. Impairment of vision.

1. The cranial deformity.

(*a*) This is characterized by the great heighth of the forehead which towers over the face.

(*b*) Feebly marked supraciliary ridges.

(*c*) Temporal ridges and depressions are feebly marked.

(*d*) A possible "crista sagittalis," a more or less prominent ridge along the sagittal suture anteriorly.

(*e*) Very high shallow orbits, the roof of the orbit being almost perpendicular and its depth being far below normal. Bertolotti's orbital index is 94 to 110 (normal 85 to 88); that is, the vertical diameter being equal or greater than the transverse diameter.

(*f*) Nasal septum deviated to one side.

(*g*) Hard palate sharply arched, narrow and frequently asymmetrical.

(*h*) Face may be asymmetrical, due usually to a flattening or depression in the malar and supramaxillary region.

(*i*) The Roentgen-ray picture is very characteristic. Much importance has been laid upon the profile of the base of the skull by Bertolotti; the turmschädel type shows a "lordose basillaire" and not a "cyphose basilaire," as is shown in dysostose-cleido-cranienne and in hydrocephalus. The middle fossa is almost upon the same level with the posterior fossa, while the sella turcica is much widened and deepened. The head sinuses are practically obliterated—particularly the frontal and the ethmoidal sinuses, while there is only a trace of the sphenoidal and mastoid cells.

The great wings of the sphenoid are flattened out and are not so vertical. Whereas the anterior projection of the opisthonbasilar line strikes 4 to 5 cm. above nasion in dysostose-cleido-cranienne and hydrocephalus, yet in the turmschädel type of deformity it strikes below nasion. The facial angle is increased from 8 to 10 degrees above the normal 54 degrees of Cuvier, though the increase is due more to the shortening of the inferior maxilla and the general "adenoid expression" of the patient, practically all of the cases being mouth-breathers.

An interesting observation is the remarkable thinning of the bones of the cranial vault and the formation of the "digital impressions" or holes on their inner surface—due undoubtedly to the pressure of the underlying convolutions. In the severe form of the turmschädel type of skull, the oxycephalic type, there is a characteristic bulging at the anterior fontanelle, usually covered by a thin layer of bone; it may be as large as a lemon, but in the majority of cases it is noticeable only upon careful observation. In all such cases of oxycephaly the "crista sagittalis" is always present. In some cases the thinning of the occipital bone advances so far as to produce an opening at the site of the external occipital protuberance, so that a definite pulsation and venous thrill can be distinctly palpated.

2. The exophthalmos with divergent strabismus and nystagmus is present in varying degrees in practically all well-marked cases; the patient may be unable to close his eyes. This exophthalmos is undoubtedly due to the very shallow orbits; Weiss and Brugger measured four turmschädel skulls which showed an orbital depth of 10 mm. less than the normal depth and 6 cm. less than the normal orbital contents. This abnormality is caused by the great wings of the sphenoid being posteriorly placed instead of externally, and by the vertical position of the roof of the orbit.

Very rarely is the strabismus convergent. The divergent strabismus is frequently unequal, the left eye being usually the more extreme.

Nystagmus is very common; it is usually bilateral and in all directions. Of the 20 cases of mild turmschädel reported by Meltzer, exophthalmos was present in 18, divergent strabismus in 19, and nystagmus in 19.

3. The impairment of vision is always the result of a secondary optic atrophy of varying degrees; it is present in practically all cases. The younger the case the better the vision, unless there is a complete optic atrophy at birth. The ability to read is rare in adults. One eye may have a contracted visual field, and the other eye be completely blind. Unless there is a total amaurosis the two eyes rarely show the same degree of optic atrophy. The picture of the beginning optic atrophy is one always seen in the later stages of brain tumor where the increased intracranial pressure has first

produced a "choked disk," and then its subsequent secondary optic nerve atrophy. This impairment of vision is usually noticed between the second and sixth years of life, progresses to a certain degree, and then stops—whether blind or not. It never produces blindness in adults.

As stated above, many theories have been used to account for this optic nerve atrophy, but it is now generally believed to be the result of the increased intracranial pressure, typical secondary optic atrophy from pressure and not a "postneuritic" condition resulting from inflammation, etc. It is most rare for the optic atrophy to be a primary one.

The loss of smell is rather frequent; Meltzer reports 12 in 20 cases. Hearing has been dulled in a number of cases. Occasionally the sense of taste is lost.

Other malformations frequently associated with cases of turmschädel deformity are:

1. Webbing of the fingers and toes (Carpenter).
2. Malformation of ears and fingers.
3. Unduly prominent internal condyle of humerus which deflects the forearm outward and may prevent complete extension (Fletcher).
4. Of 20 cases reported by Meltzer, 14 had narrow and deformed noses, while 5 had adenoid growths. Carpenter has reported the cases of two sisters (two and four years, respectively, and typically oxycephalic) who had:
   1. A systolic cardiac murmur.
   2. Webbed fingers, same type in each.
   3. Six toes on each foot and fewer number of phalangeal joints —only two as a rule.
   4. Herniæ. One sister had both an umbilical and an epigastric hernia, while the other one had an umbilical hernia.

Symptoms. The most constant symptom of this type of cranial deformity is severe headache, usually limited to the frontal and occipital regions. The child will bury its head in the pillow, holding it with both hands, and will cry almost continuously. The headache is most severe when the eyesight is rapidly failing, *i. e.*, during the time when the intracranial pressure is greatest.

Very frequently the protrusion at the anterior fontanelle and the general deformity of the head are now noticed for the first time. As the child grows older the headache may disappear entirely. It is at this early period that convulsions are likely to appear for the first time, and as the eyesight fails the "fits" become more frequent; rarely do the convulsions become chronic unless the epileptic "habit" is acquired.

Treatment. The treatment of this condition has been most unsatisfactory. A palliative expectant treatment has been followed in the cases which have been recognized as being cases of oxycephaly.

A symptomatic treatment in no way retarded the advance of the condition; the increased intracranial pressure gradually produces a secondary optic atrophy and thus blindness results; the headaches may be most severe.

Until recently no attempts have been made to relieve this intracranial pressure and thus avoid its harmful effects. This neglect has been due apparently to a misunderstanding regarding the cause of the optic atrophy, the factor of intracranial pressure having been overlooked. Some years ago von Eiselsberg trephined a case, but all trace of the patient was lost shortly after the operation. In 1911 Cushing performed four operations upon one case of oxycephaly to elevate the entire top of the head in order to lessen the increased intracranial pressure; not only were these operations quite formidable, but there was a marked tendency for the cut edges of the vault to fuse rather closely, thus tending to obviate the benefits of a permanent relief of the intracranial pressure.

It then occurred to me that the increase of intracranial pressure in cases of oxycephaly might be lessened sufficiently by a single, and if necessary a bilateral, subtemporal decompression; in early cases the operation might prevent the onset of a secondary optic atrophy and possibly produce such a lessening of symptoms and signs that a normal child would be obtained.

My first case of oxycephaly was operated upon by me at the Johns Hopkins Hospital, September 15, 1911, and has become a normal child apparently. The second case was operated upon by me at St. Luke's Hospital, Shangai, China, March 8, 1912; all trace of this child was lost shortly after the operation. My third case of oxycephaly was operated upon at the Polyclinic Hospital, New York City, April 28, 1914; this child made an excellent recovery, becoming more and more normal. My last case was an extreme type of oxycephalic deformity, and has shown a marked improvement since the operation March 15, 1915.

I offer these cases with their operative treatment in the belief that an early relief of the intracranial pressure in cases of oxycephaly will prevent the harmful effects of such pressure—headache, secondary optic atrophy with the resulting blindness and a greatly impaired usefulness.

CASES OF OXYCEPHALY. Sadonia, black, aged nine years. Born in United States. Admitted to Johns Hopkins Hospital September 14, 1911; service of Dr. Harvey Cushing.

Family History. Negative. Father died from "heart trouble" aged thirty-two years. Mother, aged twenty-nine years, living and well. No other children. Both paternal and maternal great-aunts died of tuberculosis, but none in parents' families. No cancer or rheumatism. No definite history of rickets. One uncle had convulsions at twenty-seven years, and lost consciousness, etc. No mental trouble in history.

Personal History. First child; nine months' baby; normal delivery; no instruments required. Weight, six and a half pounds. Child apparently normal at birth, except for rather large eyes. Head normal. No childhood diseases at all, other than present trouble. Six weeks after birth patient had six convulsive seizures lasting one-half hour each over a period of one month; these convulsions were thought to be due to the stomach; no fever. No recurrence until the present illness. Mild general headaches when child was five and six years of age; no vomiting; no change in shape of head observed. A bright child mentally. Eyesight said to be "hazy at times." No protrusion of eye-balls observed.

PRESENT ILLNESS. Patient was apparently in good health until twelve months ago; after complaining of frontal headaches for several weeks, she began to have severe pain in both eyes associated with epigastric pain—this latter pain apparently relieved by catharsis; at times patient vomited when headache was severe. The soreness and pain in the eye-balls has continued ever since. Some frontal headache. Attacks of dizziness were quite frequent during this period. Vision was blurred at times during the past year. Since this time the eyes have become more and more prominent, and recently there is a divergent strabismus, particularly of the left eye.

At present patient complains of pain and soreness of both eye-balls with considerable frontal headache and a sense of fulness at the top of the head and some vertigo. Mother says she has noticed the top of the head becoming taller. "Cloudy sight;" occasional attacks of nausea and vomiting; obstinate constipation.

Physical Examination. Well-nourished colored girl, aged nine years. Height, 6 m., 31 cm.

Head. An unusually tall head, the transverse diameter being apparently somewhat compressed in the biparietal region. Forehead is very high and 135 cm. above nasion is a gradually sloping protrusion to a point just posterior to the site of the anterior fontanelle on the midline. The prominence is 3 cm. in diameter and 5 cm. in height; it is smooth, with the overlying scalp quite movable. Extending forward from this prominence in the median line almost to nasion and backward along the sagittal suture toward the posterior fontanelle is a definite "crista sagittalis," very much like the keel of a boat. (It had apparently been unobserved by her parent on account of the bushy black hair of the patient.) Both the anterior and posterior sutures were firmly closed, and there was no sign of any of the cranial sutures by palpation. Mild dilatation of the veins of the scalp and eyelids, especially the upper ones.

Cranial measurements: Hat circumference (horizontal circumference), 52.5 cm., bimeatal arch, 32 cm., chin to nasion, 19 cm., width of orbit, 3.5 cm.; heighth of orbit, 4 cm.; intercanthi, 3.7 cm.; bialæ, 4 cm.

Face: Fairly symmetrical. Usual adenoid expression with divergent strabismus.

Eyes: Marked exophthalmos, particularly of the left eye; eyelids, however, can be closed with difficulty. Widely set apart. Occasional nystagmoid twitches, especially when looking to the left. Convergence very weak, especially of the left eye.

Nose: Typical negro type, flat and wide at the alæ. No deviation of septum; child prefers to breathe through mouth, though no definite nasal obstruction ascertained.

Mouth: Teeth in unusually good condition. Palatal arch very high and sharply arched; symmetrical.

FIG. 1

FIG. 2

FIGS. 1 and 2.—These figures show the prominent central protrusion at the anterior fontanelle; also the marked exophthalmos with divergent strabismus. The definite crista galli is not clearly demonstrated.

Ears: Rather low-placed, but of normal shape.

Neck: No enlarged cervical lymph nodes.

Chest: Symmetrical, equal expansion. No evidence of a rosary.

Heart and lungs: Negative.

Abdomen: Negative. No enlargement of liver or spleen. No fulness.

Extremities: Negative. Unusually free from evidences of a rachitic diathesis; no enlarged epiphyses, no curving or thickening of tibia, etc. No enlargement of internal condyle of humerus. No other abnormalities.

Neurological examination. Cranial nerves.

1. Negative. Recognized peppermint, etc.

2. Fundi. Right optic disk pale; margins irregular and clear except along the nasal margin, where there is a slight haziness. Much pigment along the temporal margins. Vessels rather full and slightly tortuous. No unusual swelling. Physiological cup shallow from new tissue formation. Left optic disk practically the same as in the right, except more tortuosity of vessels; only a small portion of the lamina cribosa is visible. Lower vessels enter the disk at its lower periphery instead of at the physiological cup. Very mild degree of secondary optic atrophy.

Vision: Practically normal. Perimeter shows a slightly contracted field of vision. Visual acuity is 14/15 in each eye.

3, 4, 6. Pupils moderately dilated, equal and react to light and accomodation. Consensual reaction good. Marked exophthalmos with divergent strabismus, especially of the left eye. Von Graefe's sign, positive. Ocular movements of left eye impaired, especially lateral movements. Convergence poor. Slight lateral nystagmoid twitches at this examination.

5. Normal. Sensation unimpaired; motor unimpaired; taste unimpaired.

7. Normal.

8. Normal. Weber's test heard equally well.

9, 10, 11, 12. Normal. Cerebrum, normal. No paralyses or anesthesias. Memory good. Cerebellum normal. Reflexes present and equal. No Babinski.

First operation, September 15, 1911. Right subtemporal decompression. Usual incision through the right temporal muscle, and the underlying bone was removed by means of the Doyen perforator and burr; bone rongeured away to a diameter of two and a half inches. Dura was normal but very tense, and upon incising it the cerebrospinal fluid spurted out. A crucial incision was made, and as the intracranial pressure tended to protrude the temporal lobe, the head was elevated sufficiently so that no injury occurred to the cortex, which appeared to be normal. Drain of rubber tissue inserted under the temporal lobe. Usual closure.

Postoperative notes: Uncomplicated recovery. Decompression site very tense. No headache at all and patient feels much relieved. Exophthalmos practically the same. To relieve the intracranial pressure still more, a left subtemporal decompression was advised.

Second operation, September 20, 1911. Left subtemporal decompression. Similar operation performed through the left subtemporal muscle; no complications. Still some intracranial pressure and the brain immediately expanded into the bony opening. Usual closure with drain.

Postoperative notes: No complications. Both decompression openings tense. The venous dilatation of the scalp and eyelids

has disappeared. Headache disappeared entirely as well as the nausea and vertigo.

Ophthalmoscopic examination revealed the disappearance of all haziness along the nasal margins of the optic disks, and a less tortuosity and fulness of the retinal vessels.

Vision practically the same. The divergent strabismus of the left eye is much less and parallelism is now fair; the exophthalmos, however, is practically the same, due, undoubtedly to the very shallow formation of the orbits. No nystagmus observed.

The protrusion at the anterior fontanelle is the same as before the operation. Since then marked improvement, apparently a normal child, except for the cranial deformity and divergent strabismus.

Letter, September 16, 1914, states: "Only two headaches since operation. In excellent health." Vision good. No nausea or dizziness.

CASE II.—Ling, male, aged four years and two months. Born in Nanking, China. Admitted to St. Luke's Hospital, Shanghai, March 4, 1912. Discharged, April 2, 1912.

Family History. Meager history obtained, negative. No history of rheumatism or cancer, but one paternal uncle had died of tuberculosis and one of "swollen feet and unable to breathe." Father had syphilis when seventeen years of age; no miscarriages or abortions apparently, father being married at the time. Nine other children living and well; two dead, one from dysentery and the other one from cholera. The patient was the seventh child. Both the mother and father had normal-sized heads, though their eyes were larger than usual among the Chinese, and four other children also had large eyes.

Personal History. Normal delivery by midwife; nine months' child; no instruments. No abnormality noted at birth—just the same as the other children. Usual diseases among Chinese children —malaria, dysentery with worms, chicken-pox. No typhoid or cholera.

Present Illness. When one year of age, patient became very irritable upon recovering from an attack of diarrhea, during which a number of worms had been expelled; for two days patient cried practically all of the time and did not sleep. Two weeks later a small lump was noticed on the top of the head (at the site of the anterior fontanelle); after four weeks it gradually increased in size to that of a small plum. During this time, patient held its head in its hands and cried very much, especially at night. This continued for one month, and then child became apparently less fretful and apparently normal, except for the lump upon the top of the head. At two years the large eyes of the child were observed apparently for the first time, and during the past two years they have become very large, protruding over half-way beyond their

equator; extreme divergent strabismus, especially of the left eye which is also turned upward. Hearing also has become defective during the past two years. Occasional attacks of headache, but not so severe as at first. No nausea nor vomiting at any time. Child has become absolutely blind during the past year—even for light.

Until six months ago child apparently as bright and quick as the other children, but during the past few months, child has become very quiet and rather sleepy. Still plays, however, with its sticks, but less actively than before. Apparently no paralyses.

Physical Examination. Well-nourished Chinese boy, aged four years. Color good.

Neck: No enlarged lymph nodes.

Chest: Negative; symmetrical; equal expansion. No rosary. Heart and lungs negative.

Abdomen: Rather full, but symmetrical. Liver and spleen negative.

Extremities: Negative. Radial epiphyses not enlarged. Internal condyle of humerus, negative. Tibia, both round; no bowing. One undersized testicle, left.

Head: Tall and rather broad in temporal region, so that head tapers toward the vertex. Forehead high but slopes gradually backward. Veins of scalp and eyelids dilated. At the site of the anterior fontanelle is a bony enlargement, the size of a small lemon, 3.5 cm. wide and 2 cm. high, directly in the midline; its bony covering rather bends slightly under firm pressure; the sagittal suture is elevated slightly, both anteriorly and posteriorly of this protrusion. Posterior fontanelle closed and the other suture lines cannot be palpated.

Face: Non-symmetrical; the left molar arch less prominent than the right; nose, however, is not deflected and is a typical Chinese nose, rather flat and delicate.

Eyes: Extreme proptosis, with divergent strabismus, especially of the left eye. Slight conjunctivitis of both eyes. Both eye-balls can be easily shoved forward by forefinger in the external canthus, practically dislocating each eye; apparently this procedure is not painful. No vision at all in either eye, not even to light apparently.

Ears: Both rather low set, possibly only relatively; well formed.

Mouth: Teeth good. Palate high arch and asymmetrical, deflecting toward right.

Throat: Negative, except for slightly enlarged tonsils. Child, however, is a mouth-breather.

Neurological Examination. Cranial nerves.

1. Negative as well as could be ascertained.

2. Typical secondary optic atrophy in both eyes, practically the same. Dull whitish optic disks with irregular margins, physio-

logical cup filled with scar tissue. Veins full and tortuous. No increase of pigment. Vision apparently absolutely *nil.*

3, 4, and 6. Extreme exophthalmos with divergent strabismus, especially of the left eye. Pupils widely dilated and do not react to light directly or consensually. All voluntary movements of eye-balls has practically been lost, except slight movements upward and downward and at times to the right. No nystagmus ascertained.

5. Negative.

7. Negative.

8. Very hard to ascertain, but certainly not so acute on both sides as normally.

9, 10, 11 and 12. Negative.

Cerebrum: Still a bright child but rather dulled apparently.

Cerebellum: Negative.

Reflexes: No exaggeration; all of them obtained, equal.

Treatment. For fear that the child would gradually become more and more dulled and possibly an imbecile, and also to relieve the headache, I advised a double decompression in spite of the complete secondary optic atrophy; after much difficulty consent was obtained.

Operation March 8, 1912. Father and two brothers insisted upon being present. Right subtemporal decompression. Usual incision made and bone removed; no complications. The vault was very much thinned and revealed the "digital markings" so frequently observed in skulls subjected to high intracranial pressure. The cerebrospinal fluid was under great tension so that it spurted three inches when the dura was incised. After much cerebrospinal fluid had drained away the brain became less tense and pulsated normally. I inserted a strip of rubber tissue beneath the right temporal sphenoidal lobe as in fracture cases and then made the usual closure; no complications.

Postoperative notes: Uncomplicated recovery. Drain removed upon second day. Child apparently in no discomfort. No improvement in the exophthalmos nor divergent strabismus, but the dilatation of the veins of the scalp and eye-balls almost completely disappeared. Fundi retinal veins less dilated.

Fifth day: No headache. Mother thinks child brighter mentally.

Sixth day: During the night, the father came to the hospital with a carriage, and forcibly removed the child, for fear of a second operation.

No photograph had been obtained due to objection of the parents —they were always with the child and they feared an "evil spirit." No trace of the child has been secured.

Case III.—Bernard, aged ten years. Diagnosis: Mild type of oxycephaly. Operation, right subtemporal decompression. Admitted to Polyclinic Hospital April 27, 1914.

Family History. Father and mother alive and well; father has rather large head, high and long. One brother and one sister alive and well. One brother a twin. No miscarriage. No history of abnormally shaped heads or usual disturbances.

Personal History. Fourth child; last twin; very long delivery; no instruments used, however. Apparently normal baby, although the large head was noticed at birth. At two years and three months of age, patient had a convulsion: "Was deaf, dumb, paralyzed, and blind for three weeks; high fever." The convulsions at this time were the first patient had had, lasting one and a half days. Since then patient has had about fifty in all, occurring at irregular intervals, one week to three months. These convulsions have been getting worse and more frequent; last week one, week before one, and one today. No prodromal signs; begins with both hands, then legs and lips; often froths at mouth; sometimes bites tongues; convulsion lasts about one hour. Unconscious during spell; afterward weak for several days. Head is gradually becoming larger at the top in front, and more noticeable; deformity increasing in region of forehead. Anterior fontanelle closed at three years of age. Patient is in school in 2B but teacher says he is only fit for 1A. Not at all bright, apparently unable to learn. Likes to roam streets and fights willingly. Talks, but not very well. Very poor memory. Sleeps normally. Bowels regular. Patient has been very unruly, and is becoming worse. Frequent headaches, at times accompanied by nausea and vomiting. Complains of gradual haziness and blurring of vision; sees double at times. Restless; irritable.

Physical Examination. Rather prominent sternal angle; suggestion of "rosary;" some enlargement of lower radial epiphyses. Patient has characteristic "towering" frontal bone; no marked protrusion of the anterior fontanelle.

Measurements: Circumference (hat band), 55 cm.; bimeatal arc, 38 cm.; nasion-basion arc, 40 cm.; basion mental diameter, 18 cm.; basion-nasion diameter, 17½ cm.; biparietal diameter, 14 cm.; bifrontal diameter, 10 cm.; bizygomatic diameter, 10 cm.; bi-external canthus, 9 cm.; bi-internal canthus, 2½ cm.; palate width, 3 cm.; nasion-mental arc, 10 cm.

Reflexes: Active but not unequal; no Babinski, although no plantar flexion of toes obtained. No paralyses. Pupils equal and react normally. A divergent strabismus observable at times, the right eye more than the left; rather prominent large eyes but no definite ptosis or proptosis. Definite lateral nystagmus—greater toward left. Fundus examination reveals a dilatation of the retinal veins and a distinct blurring of the nasal halves of both optic disks; the physiological cups are shallow, being filled with edematous new tissue formation, an early stage of secondary optic atrophy and the cause for the impairmant of vision. A subtemporal opera-

tion was advised to lessen the intracranial pressure and thereby not only preserve the vision, but avoid the headaches, and possibly lessen the convulsions and improve the mentality.

Operation, April 28, 1914. Right subtemporal decompression. Usual incision and removal of bone; no complications. Dura quite tense and upon incising cortex, tended to protrude. Large quantity of cerebrospinal fluid escaped. Cortex itself normal. Dura not thickened except slight congestion due to tension; no adhesions. Usual closure; drains. No complications.

Condition at discharge, May 10, 1914. Uneventful convalescence. No convulsions while in hospital.

FIG. 3.—The protrusion at the anterior fontanelle is broad, so that the entire anterior portion of the vault is enlarged, resembling the extreme type of turmschädel deformity.

April 2, 1915. (One year after operation.) Mother says patient is "better in every way since operation; quiet; more sense." No convulsions at all, but patient has had fifteen momentary lapses of consciousness, not sufficient to cause patient to fall (undoubtedly petit mal attacks). No headache at all. Patient seems more observant and has advanced in school. Site of operation flush with surrounding scalp, but tense.

June 19, 1915. Improvement continues. No convulsions and no momentary loss of consciousness during the past six weeks. No headaches. Vision not impaired.

February 4, 1916. Patient is apparently becoming a normal boy. His school work has markedly improved. No convulsions at all—not even the momentary lapses of consciousness. No complaints. Decompression area, however, is still tense, but it does not protrude.

CASE IV.—Isadore, aged fifteen years. Diagnosis, oxycephaly. Operation, bilateral decompression. Admitted to Polyclinic Hospital March 14, 1915.

Family History. Negative. No history of abnormally shaped heads nor visual disturbances. Two brothers and sisters well and strong.

Personal History. Third child; full term; difficult labor; instrumental. Nursed normally. Scarlet fever at four months of age; apparently excellent recovery; could walk and talk at two years of age. Child seemed perfectly normal up to two and a half years of age, when it was noticed that the head was peculiarly shaped at the

FIG. 4.—A lateral Roentgen-ray on the tenth day after operation; the circular grayish area represents the decompression opening with the small silver clips attached to the dural vessels. The protrusion at the anterior fontanelle with a definite thinning of the adjacent vault can be observed.

top; child cried a great deal, holding its head in its hands. No trouble was suspected, however, until sight began to fail at four years of age. Sight gradually failed, and at five years it was so poor that he could not be sent to public school. At seven years he was just able to distinguish light and darkness and tell when an object was in front of him. At ten years he attended a school for the blind and learned, very rapidly, reading, writing, spelling, geography, history, typewriting, etc. Patient is very bright and at time of entrance to hospital was in last grade of public school.

Reads rapidly (including works of Shakespeare) by means of raised print, and plays checkers with considerable skill. Has learned some carpentry work and has made several articles of wood. Occasional headaches and shooting pains in the head, otherwise no complaints.

Physical Examination. Fairly well developed and nourished. No signs of rickets. Right arm slightly atrophied, particularly over bicipital and deltoid regions; head held slightly bent forward. Typical "adenoid" expression and the throat reveals some adenoid tissue. Rather high, narrow, arched palate. Heart, lungs, and abdomen negative.

Head measurements: Circumference (hat-band), 50 cm.; bimeatal arc, 36 cm.; nasion-basion arc, 35 cm.; occipitomental diameter, 20 cm.; basion-nasion diameter, 20 cm.; basion-nasion diameter, 18 cm.; biparietal diameter, 14 cm.; bifrontal diameter, 13 cm.; bizygomatic diameter, 13 cm.; bi-external canthus, 9 cm.; bi-internal canthus, 3 cm.; palate width, 4 cm.; Apex of nose-mental arc, 23 cm.; nasion-mental arc, 13 cm.

Eye examination by Dr. Kearney March 15, 1915. Definite ptosis and divergent strabismus, left greater than right; definite proptosis of both eyes, right probably greater than left. Eyes stare. Other external conditions normal except in dilatation of the palpebral vessels. Pupils regular, equal and do not react; slightly enlarged. Media clear. Fundus, picture of secondary optic atrophy; practically complete in both eyes. Optic disks both white; margins on lower and temporal side clearly cut. Upper and nasal margins broken down with scar-tissue formation. Cupping slightly exaggerated. Arteries and veins bear normal relations as to size, kinking noted in smaller branches. Fundus tesselated, lighter streaks showing choroidal circulation beneath. Definite lateral course nystagmus—greater toward right.

Reflexes. Abdominal reflexes equal and active. Knee-jerks slightly exaggerated but equal. No ankle-clonus; no definite Babinski, though suggested on both sides. No Oppenheim, Gordon, or Chaddock. Wassermann test of blood negative. Wassermann test of cerebrospinal fluid negative; six cells; no globulin.

Lumbar puncture (March 14, 1915): Pressure of cerebrospinal fluid, 37. Elevate head, 41. Lower head, 36. Cough, 38. Blood-pressure, 110 before, 125 after.

Operation March 15, 1915. Right subtemporal decompression. Usual incision and bone removed; no complications. Bone exceedingly thin in places, being the digital depressions due to high intracranial pressure forcing the convolutions into the bone, somewhat like depressions of Pacchionian bodies. Dura very tense; otherwise normal, being thin, transparent, not vascular, no adhesions. Cerebral cortex under high pressure tended to protrude upon incising the dura; not edematous. Along the cortical veins, how-

ever, were some areas of whitish induration. Effort to puncture, ventricles and thereby lessen tension not successful. Usual closure with drains; no complications.

Postoperation, first day: Drain removed. Wound bulging slightly but pulsating. Boy talking brightly. Has no pain.

Third day: Several sutures removed; wound healing nicely. Boy distinguishes light from darkness much more readily; could tell for first time in many months when electric light was lighted before him.

Fifth day: All sutures removed. Boy up and about. Very active.

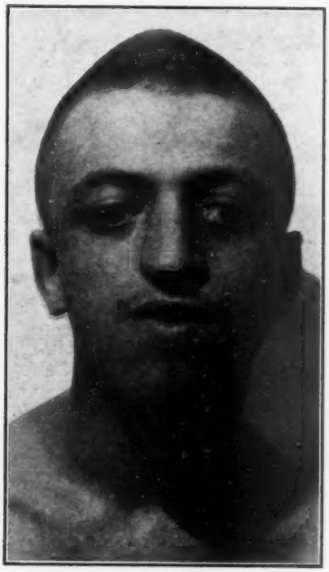

FIG. 5.—The marked pointed protrusion at the anterior fontanelle is very striking; the crista galli is also present. The divergent strabismus is greater to the left.

Seventh day: "Reading" his Shakespeare and playing checkers cleverly with other patients.

Ninth day: March 24, 1915. Patient discharged.

April 12, 1915. Second operation. Left subtemporal decompression. Usual incision, bone removed and exceedingly thin in places, showing typical digital depressions which were the most marked of any I have yet seen. The dura was thickened with many adhesions overlying the bone; exceedingly tense, and upon incising it the cortex tended to protrude at the lower part of the dural opening, the cortex causing a slight hernial protrusion. An unusually large decompression opening was made, two and a half to three inches in diameter.

The ventricle was tapped, allowing a small amount of cerebrospinal fluid to escape, thereby lessening the cortical tension, which subsequently pulsated normally. Usual closure with small rubber tissue drain.

Postoperation. Negative.

Discharged April 20, 1915, eight days postoperative.

May 16, 1915. No complaints other than blindness; patient, however, can still tell the presence of light or not. No headaches.

FIG. 6.—A lateral Roentgen-ray on the twelfth day after the bilateral decompression operation; the circular darkened areas are the decompression openings. The protrusion at the anterior fontanelle with the marked thinnings ("digital depressions") of the vault due to the high increase of the intracranial pressure are clearly shown. The lordosis at the base of the skull is evident.

June 19. Condition about the same. Vision unchanged. No headaches.

February 8, 1916. Patient states that he can see better—moving objects, bright colors, etc. This is confirmed. Counts fingers if held very close to eyes. This improvement of vision was not expected, as the condition of secondary optic atrophy was believed to be complete. No headaches; no complaints. Patient is studying Latin, algebra, etc., in the De Witt Clinton High School of New York City.

TURMSCHÄDEL TYPE OF SKULL; NO OPERATION.

CASE I.—Gottlieb, aged forty-five years, married. German Jew.

Family History. Negative. Father (Rector of the University of Prague; professor of mathematics and astronomy) died, aged seventy-two years of senility; mother died aged forty-nine years, of "dropsy;" two brothers living and well; two sisters living and well. Seven brothers and sisters dead—one of consumption, three in infancy, three of unknown causes. Sister has rheumatism. No history of cancer, gout nor of any nervous disease; nor of lues and rickets. Apparently no large head nor large eyes in family history.

Personal History. Nine months' child; weight seven and a half pounds. No instruments; head normal apparently. Always well and strong. Very bright and active child; no intellectual impairment. Always stood at the head of his class (University of Prague); A.B. degree and student of medicine; traveled through Europe as tutor. No childhood diseases.

Habits: Always a hard-working, strenuous student; a strenuous life. Occasional glass of beer at night; heavy tobacco smoker.

Neuromuscular negative. Weight, 192 pounds.

Present Illness. When a child, patient had frequent severe frontal headaches, beginning as early as he can remember, and occurring every four or five months; they are, however, of the same character. Patient thought they were due to a blow upon the head, causing the present cranial deformity.

Left facial neuralgia of much severity daily, especially the upper two branches of the nerve; an alcohol injection one year ago brought relief until four weeks ago, when the pain returned, not very severe.

Sharp, shooting pain in both eyes, ever since patient can remember and especially when he was eight or nine years of age; some radiation of pain upward and outward. This pain occurs each day, and at times has a "burning sensation," making eyes water considerably.

Eyes have protruded slightly ever since childhood, and most noticeable at the age of eight years, and especially the left eye, which turned outward. Patient says he is color blind for red. Occasionally sees double when trying to focus with the left eye, false image being to the right. Vision not so good in the left eye, the same for years. Vertigo at times, subjective.

Physical Examination. Well-nourished, rather obese white man. Ruddy complexion with the typical Semitic facies. Mucous membrane of good color. Apparently in the best of health. Intelligence excellent.

Chest symmetrical; equal expansion. No rosary. Heart and lungs negative.

Abdomen symmetrical; pendulous. Liver and spleen negative. No free fluid.

Extremities negative. No enlargement of radial epiphyses or internal condyle of humerus.

Head large, turmschädel type of skull very high and broad and tapering upward posteriorly to the vertex. No oxycephalic protrusion at the anterior fontanelle. Forehead retreating, but high. The right side of the skull up to the middle line is more prominent than the left side. No venous dilatation of scalp or eyelids, except at the external canthus of the right eye. Cranial sutures cannot be palpated.

Pupils equal and react rather sluggishly to light. Von Graefe's signs mildly positive. Diplopia upon looking to the left and focussing with the left eye. Slight nystagmoid lateral twitches—equal in both directions.

Fundi mild secondary optic atrophy; retinal veins somewhat dilated; physiological cup shallow; optic disks pale with irregular margins. Frequent nosebleeds as a child, no traumatism. Sense of smell normal.

Ears negative. No discharge or ache.

Patient at present is better than he has been for years. Really no complaint at all, other than the slight facial neuralgia. Naturally no operation advised.

Conclusions. Cases of cranial deformity of the oxycephalic type are fairly common and are usually brought first to the ophthalmologist on account of the failing vision due to a secondary optic atrophy of varying degree. In my opinion the condition is primarily due to an early meningeal irritation, with the resultant premature closure of the sutures of the base and posterior portion of the skull; as the brain enlarges it tends, therefore, to protrude through the anterior fontanelle and thus the characteristic cranial deformity is produced, and as the result of the increased intracranial pressure a choked disk with the consequent secondary optic atrophy occurs.

The treatment should be directed toward a relief of the increased intracranial pressure; in the cases of the turmschädel type of deformity of the skull there is usually no visual impairment, and the cranial deformity is slight because the intracranial pressure is not high; these cases do not require an operation.

In the oxycephalic type of cranial deformity, however, the increased intracranial pressure should not be allowed to produce the blindness of a secondary optic atrophy; an early relief of this increased pressure with the resulting avoidance not only of the cranial deformity but of the far more important impairment of the vision is advisable by means of the operation of cranial decompression; of the cranial operations to be used, the subtemporal decompression is the operation of choice.[1]

[1] The Operation of Cranial Decompression, Am. Jour. Med. Sci., April, 1915, No. 4, cxlix, 563.

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OBSERVATIONS ON THE CUTANEOUS TUBERCULIN REACTION IN THE TUBERCULOUS.

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Hypersensitiveness to tuberculin when introduced into the body previously infected with the tubercle bacillus has been a recognized fact since Koch's first use of this bacillary extract in 1890. At first only general hypersensitiveness was recognized,

and it remained for von Pirquet, in 1907, to demonstrate local or skin hypersensitiveness. Later it was shown that the mucous surfaces, the eye, etc., also reacted in a hypersensitive way when tuberculin was locally administered, so that now it is assumed that all organs and tissues of a person once infected with the tubercle bacillus will show specific inflammatory or hypersensitive reactions when tuberculin is given locally. The nature of the phenomenon is not thoroughly understood. In a general way, however, it may be said that when the tubercle bacillus gains entrance to the body and incites a local reaction, or, in other words, induces a focus of infection, the body responds in a protective way with the formation of what in a general way may be termed "antibodies" to the poisonous products of the tubercle bacillus. The antibodies are at first circulating, or shortly become so, and are carried to all portions of the body, later to become fixed in the cells of the various tissues, and when tuberculin (antigen) is introduced locally in sufficient quantity an inflammatory reaction occurs. Under certain conditions such as the existence of an acute infection, notably measles or in the last stages of a progressive tuberculous infection, the local hypersensitive reaction fails to occur. Thus in a measure the reaction may be looked upon as an evidence of resisting power on the part of the host.

Unfortunately the greater proportion of all individuals have at one time been infected with the tubercle bacillus, so that the various tests based on this hypersensitive reaction will prove positive in the greater proportion of individuals when tuberculin in sufficient concentration is used. That a focus of infection need have existed before tuberculin will give rise to hypersensitive reactions has been denied by some, notably Much, Sata, etc. However, other observers have claimed to get no hypersensitive reactions unless a lesion has existed. These tests have all been done by the subcutaneous or intravenous injection methods and refer to general hypersensitiveness only. Hamburger, Baldwin, Poten, Roemer, Giemert, Joseph and others come to the latter conclusion. And, too, a few observers have presumably been able to demonstrate a loss of hypersensitiveness after removal of an existing focus, viz., Bahrat, Felix, Klemperer. However, some of these latter tests have been based solely on temperature reactions in guinea-pigs and are not conclusive. The general opinion, however, is that an infection must have taken place before the body in general will react in a hypersensitive manner to tuberculin. And upon this reaction are based the several tests for the existence of a previous infection with the tubercle bacillus. Whether or not the tests have a larger application and will give other information regarding the reaction on the part of the host is yet an undecided question. Lawrason Brown, in a series of 200 cases, could establish no other definite relation.

Ellerman and Erlandsen, in 1909 and 1910, published their observations with a new technic by which they were presumably able to differentiate active, inactive, and latent tuberculosis. The von Pirquet method was used and the strength of tuberculin varied in geometric progression. For instance, four punctures were made, and tuberculin in 1 per cent., 4 per cent., 16 per cent., and 64 per cent. dilutions were applied. Measurements of the papules were made after twenty-four and forty-eight hours, and the average size of the papules and the average differences in papule sizes were calculated. From these figures the hypersensitiveness was determined. This is, according to Morland, really the inverse of the lowest strength of tuberculin causing a reaction. A hypersensitiveness of 100 was said by Ellerman and Erlandsen to be the dividing point between active (100+) and inactive (100—) tuberculosis. Erlandsen and Petersen and Mirauner published their observations in substantiation of the Ellerman Erlandsen method, and Mirauner would include in the active class all who showed a hypersensitiveness of over 50.

On the other hand, Bessaun and Schwenke think that the clinically tuberculous show no hypersensitiveness, but when it does occur it denotes a favorable prognosis. And when hypersensitiveness fails to increase it is of doubtful prognosis. Pringsheim comes to practically the same conclusion.

Hamburger, by repeating tests at intervals, comes to the conclusion that hypersensitiveness increases gradually in early cases, remains low in mild cases, may increase markedly and suddenly when the process becomes active, and disappear slowly when the disease rapidly progresses; and that when hypersensitiveness increases, the prognosis is good and may be an indication for the use of tuberculin.

Among the tests used for determining skin hypersensitiveness is that of Mendel, Mantoux, and Roux, the so-called intradermic test. In this method tuberculin is injected between the layers of the skin, and it has the advantage that a definite quantity of tuberculin can be used with the assurance that it is all absorbed. Thus it affords an excellent method for determining more closely the amount of tuberculin necessary to cause a local reaction. Pringsheim, Jeaneret, Holmes and others worked with the intracutaneous test. Pringsheim used fresh solutions, 1 to 100, 1 to 1000, and 1 to 10,000, and gave the tests eight days apart. In his conclusions he mentions that 10 per cent. of the von Pirquet tests done simultaneously failed to react parallel to the intracutaneous. He also states that 76 per cent. of clinically non-tuberculous children show hypersensitiveness. Holmes showed that activity of the focus increased hypersensitiveness locally. Rosenberg found that 100 per cent. of clinically tuberculous and 62 per cent. of non-tuberculous reacted to a dilution of 1 to 50,000, while 94 per cent.

of clinically tuberculous and 25 per cent. of non-tuberculous reacted to a dilution of 1 to 500,000, and from this he concludes that failure to react to the dilution of 1 to 500,000 would exclude clinical tuberculosis. Kogel says that a strong reaction with a high dilution indicates that healing processes are taking place. Jeaneret comes to the conclusion that the intradermic reaction is in a general way an indication to the grossness of the focus. He also believes that a strong intradermic reaction in a case showing few physical signs is a contra-indication for the use of tuberculin.

Ostenfeld and Permin, in an analysis of 56 cases of skin reactions find that the reactions bear in no definite way on the activity or extent of the disease.

And so conclusions are at variance and the truth not fully understood.

A series of intradermic tests were studied by us at the Adirondack Cottage Sanitarium in an effort to find any existing relation between the quantity of tuberculin necessary to incite a reaction of a certain size and the stage of the disease.

The intradermic reaction was chosen because it allowed more accurate dosage than any other method of skin test. The skin of the forearm was always the seat of the injection, and 1/10 c.c., the volume of solution, remained always the same. Koch's O. T. was the tuberculin invariably used, and care was taken that the injection was always between the upper layers of the skin and that the bevel of the needle could be seen through the skin. The quantity of tuberculin, however, was increased ten times at each successive injection until an erythema of an average diameter of 20 mm. or more was produced. Measurements were taken twenty-four and forty-eight hours after injection.

For convenience the dose is expressed in the form of a fraction as suggested by Dr. Lawrason Brown. The numerator specifies the number of zeros after the decimal point in the metric system, and the denominator the actual amount of tuberculin. Thus 0.0000001 c.c. would be recorded $\frac{6}{1}$ c.c.

Each patient was at first given an intradermic test with $\frac{6}{1}$ O. T. or less, and at the end of three or four days, provided a reaction of sufficient degree was not attained, this dose was increased ten times ($\frac{5}{1}$ c.c.). And if this dose failed to produce the required erythema it was again increased ten times ($\frac{4}{1}$ c.c.), and so on until an erythema of 20 mm. or more average diameter was produced. It was thought inadvisable to produce a greater erythema than this, inasmuch as the attempt in two instances was coincident with a slight general reaction.

The series was made up of 200 cases, including mostly incipient and moderately advanced cases (3 far advanced). And the reactions were studied in relation to (1) the stage of the disease; (2) the presence or absence of tubercle bacilli, also of rales; (3) the manner

of onset of the illness; (4) the progress of the case in the sanitarium; (5) the probable duration of the disease.

In general it may be said that those cases having both rales and bacilli showed a greater hypersensitiveness to tuberculin than those cases in which neither rales nor bacilli were present, and that the hypersensitiveness was more marked in the moderately advanced cases.

The majority of cases (84 per cent.) reacted to either $\frac{2}{1}$, $\frac{3}{1}$, or $\frac{4}{1}$, and the majority of these (34.5 per cent. of the total) reacted to $\frac{3}{1}$. Using $\frac{3}{1}$ as the dividing point and watching the direction of the increase in percentages for the different quantitative reactions, we find:

1. That there is a tendency for the moderately advanced case to react to a smaller quantity of tuberculin than the incipient, though the difference in percentage (6 per cent.) is too small to warrant any accurate conclusions.

2. That when tubercle bacilli are present in the sputum the percentage of all cases reacting to less than $\frac{3}{1}$ is 19 per cent. greater than when tubercle bacilli are absent (47 to 28). And that the difference in reaction is more noted in the incipient cases (48 to 27). Moderately advanced, 47 to 30.

3. That when rales are present on physical examination the percentage of all cases reacting to less than $\frac{3}{1}$ is 19 per cent. greater than when rales are not present (44 to 25). And that the difference in reaction is about the same for incipient and moderately advanced cases. Incipient, 42.5 to 24; moderately advanced, 40 to 22.

4. That when both rales and bacilli are present the percentage of all cases reacting to less than $\frac{3}{1}$ is 26 per cent. greater than when neither bacilli nor rales are present; and that the difference in reaction is about the same for incipient and moderately advanced cases. Incipient, 47 to 21; moderately advanced, 45 to 20.

5. That 36 per cent. of all cases react to less than $\frac{3}{1}$. That this percentage is increased most markedly when the onset has been hemoptoic (51 per cent.) or catarrhal (40 per cent.). And that the percentage is reduced when the onset has been insidious (26 per cent.), febrile (25 per cent.), and pleuritic (24 per cent.), the last three having almost the same percentage.

6. That the greater percentage reacting to weaker dilutions occurs when the onset is:

Insidious in the incipient cases (incipient 35 per cent. to moderately advanced 22 per cent.).

Catarrhal in the moderately advanced cases (moderately advanced 50 per cent. to incipient 31 per cent.).

Hemoptoic in the moderately advanced cases (moderately advanced 60 per cent. to incipient 40 per cent.).

When the onset is pleuritic the percentage of cases reacting to less than $\frac{3}{1}$ is about the same in both incipient and moderately

advanced cases. The cases with febrile onset were too few to be considered (4).

7. Considering the reaction from the standpoint of prognosis, that is, the relation of the reaction to the progress of the case while in the sanitarium, we find that:

Of the apparently arrested cases, 22 per cent. reacted to less than $\frac{3}{1}$.

Of the quiescent cases, 42 per cent. reacted to less than $\frac{3}{1}$.

Of the improved cases, 36 per cent. reacted to less than $\frac{3}{1}$.

Of the unimproved cases, 35 per cent. reacted to less than $\frac{3}{1}$.

The percentage of incipient and moderately advanced cases reacting to less than $\frac{3}{1}$ was approximately the same when the cases were apparently arrested or quiescent.

Apparently arrested (incipient 22 per cent.; moderately advanced, 23 per cent.).

Quiescent, (incipient, 45 per cent.; moderately advanced, 40 per cent.).

The incipient improved cases showed 25 per cent. fewer reacting to less than $\frac{3}{1}$ (21 per cent. to 46 per cent.), and the incipient unimproved cases showed 11 per cent. more reacting to less than $\frac{3}{1}$ (40 to 29 per cent.) than of the moderately advanced cases.

Considering the apparently arrested and quiescent cases as probably having passed the border-line of activity of their disease at the time of the test, and the improved and unimproved cases as being on the border-line of activity, we may possibly assume that the cases with little involvement, as they improve, lose, and as they get worse, gain, in hypersensitiveness; whereas, the case of longer standing and more advanced disease, on improving, gains, and on not improving, losses in hypersensitiveness. Of course this can only be an assumption.

When the cases are considered purely from the Turban found on physical examination, the percentages reacting to less than $\frac{3}{1}$ are approximately the same for I, II and III (36 per cent., 34 per cent. and 30 per cent.), but the curve of hypersensitiveness appears to become greater as the Turban increases, for: 34 per cent. Turban I, 23 per cent. Turban II, and 8 per cent. Turban III, react to more than $\frac{3}{1}$, the percentages reacting to $\frac{3}{1}$ increasing as the Turban increases (30 per cent., 38 per cent., 62 per cent.).

When the cases are considered from the standpoint of the duration of the present illness, we find practically no variation in percentages reacting to less than $\frac{3}{1}$, when incipient and moderately advanced cases are compared.

Conclusions. 1. The nature of the focus of infection at the time of the test influences local hypersensitiveness.

2. The quantity of tuberculin necessary to incite a local reaction of 20 mm. diameter bears no definite relation to the stage of the disease. Therefore a single skin test when positive means nothing but the existence of a previous infection.

NON-TERATOMATOUS BONE FORMATION IN THE HUMAN OVARY.[1]

By George W. Outerbridge, M.D., F.A.C.S.,

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In 1912 two French surgeons, Pozzi and Bender, published a paper in which they discussed at some length the question of bone formation in the ovaries and Fallopian tubes other than that of teratomatous origin, and reported two personal observations of this condition in the ovary. They also stated their belief that such ossification of the ovary is of extremely rare occurrence, since they were able to find in the literature mention of but 5 additional cases which they considered reasonably authenticated, although in a number of other instances specimens had been reported as falling in this category which on investigation were found to have been too imperfectly studied to be accepted. These 7 definite cases are divided by Pozzi and Bender into the following groups: 2 ossified ovarian fibromata, 2 ovarian cysts with ossification of the walls, 2 cases of diffuse ossification in sclerotic ovaries, and 1 ossified corpus luteum.

Since two cases of ovarian ossification happened to come under my observation shortly after the appearance of Pozzi and Bender's article, I was rather surprised by their statement as to the extreme rarity of the condition, and was somewhat skeptical of the accuracy of this view. A fairly careful search through the literature, both antedating and subsequent to their paper, has brought to light a few additional reports, bringing the total of what may be considered fairly well-authenticated cases up to about 14. While this may not represent an absolutely complete list, the number of reports is certainly surprisingly small in view of the considerable amount of literature which exists upon the subject of abnormal ossification in other portions of the body.

The occurrence in ovaries of little hard nodules, often called "ovarian stones," is well recognized as a not exceedingly infrequent phenomenon, but these are usually considered merely calcareous deposits in sclerotic ovaries or degenerated corpora lutea, and are probably in most instances never subjected to microscopic examination, without which the definite determination of the presence of bone is hardly possible. In order, therefore, to ascertain whether or not the occurrence of true bone in the ovary (aside from that formed in dermoids and solid teratomas) is really as unusual as

[1] Presented before the Pathological Society of Philadelphia, May 13, 1915.

has apparently been assumed, I have subjected to microscopic examination, after thorough decalcification, sections from all ovaries containing hard nodules which have come into my hands. In this manner 7 specimens have been studied, with the result that areas of true bone have been found in every one, sometimes of greater extent, sometimes, of lesser, but always clearly demonstrable. The material was derived from the following sources: 5 cases from the gynecological service of the Hospital of the University of Pennsylvania (Dr. John G. Clark), 1 case from the Gynecean Hospital (Dr. Henry D. Beyea), and 1 case from the gynecological service of the Methodist Hospital (Dr. William R. Nicholson). In every instance microscopic examination of sections taken from various areas failed to reveal anything suggestive of a teratomatous process.

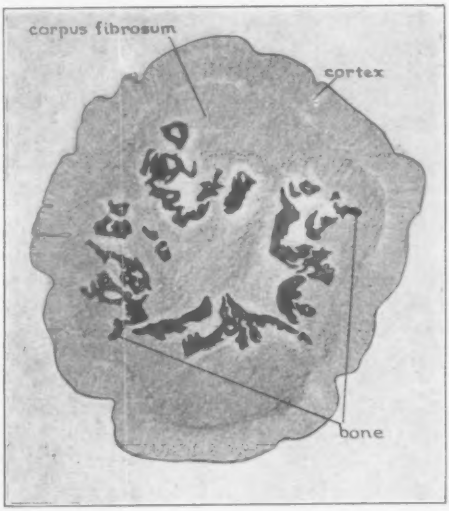

FIG. 1.—Case I. Sketch-drawing of section through the entire nodule. Very low power.

CASE I.—U. Pa., No. 2261. This patient, a girl, aged twenty years, was operated upon by Dr. Clark in 1909, during my term of internship on his service at the University Hospital. The left ovary was somewhat cystic and the right contained a small, very hard nodule. A partial resection of each ovary was performed, with removal of the appendix. The specimen received at the laboratory consisted of "the wall of a corpus luteum hematoma from the left ovary, with a firm, calcified mass, measuring 1.7 x 1.6 x 1.4 cm., from the right;" no histological examination of the hard nodule was originally made, merely a diagnosis of "right

oöphoritis interstitialis chronica (with calcareous degeneration)" being returned by the pathologist. On becoming interested in this investigation I looked up the specimen and found the little nodule intact. Owing to the length of time it had lain in preserving fluids, decalcification was difficult and the soft parts had lost much of their staining properties; the sections obtained, although clearly showing the presence of true bone, were hardly satisfactory for photomicrographic purposes, and therefore merely a sketch drawing of the entire section through the nodule is presented, to show the relations between the ovarian cortex, corpus fibrosum, and the numerous areas of bone forming an incomplete ring or shell within the circumference of the latter (Fig. 1). The tissue in the centre of this bony ring is somewhat looser in structure than that forming the outer portion of the corpus fibrosum, external to the bone. The latter is arranged in wavy, more or less parallel lamellæ, with rather sparse bone bodies; the structure is distinctly compact, but without any very definite Haversian systems.

Summary. This case presents an example of ossification within a corpus fibrosum; the ovary was otherwise normal, and there were no marked inflammatory changes in the pelvic organs.

Case II.—U. Pa., No. 3478. Aged forty-six years. *Clinical diagnosis:* pelvic abscess; pelvic inflammatory disease; tuboövarian abscess. *Operation* (Feb. 7, 1913): vaginal puncture; supravaginal hysterectomy; bilateral salpingoöphorectomy. *Specimen:* myomatous uterus; large right tuboövarian abscess; left hydrosalpinx; *left ovary.* The latter measures 4 x 2.5 x 2 cm.; it is closely adherent to the outer end of the tube, and on section is seen to contain a large degenerating corpus luteum, in which is a considerable area of bony hardness. *Microscopically,* the left ovary shows a fairly normal cortex, closely fused with the wall of the pyosalpinx (Fig. 2). The most prominent feature of the specimen is a good-sized corpus fibrosum, which in some sections shows an almost complete ring or shell of deeply staining calcareous material, with a few small but distinct areas of bone along its inner border. The central area is filled with a loose, richly vascularized tissue, with considerable interstitial hemorrhage. In other sections, cutting through a slightly different plane (Figs. 3 and 4) extensive masses of bone are seen running all through this central softer tissue, which here presents an appearance strongly suggestive of marrow. The bone appears to have formed in the central cavity of the calcareous shell, with which it is everywhere in intimate relationship (Fig. 5). It is fairly compact, with numerous bone bodies in small lacunæ, and indications of Haversian system formation, although this is not very distinct.

Summary. This case presents an example of ossification within a fairly extensive calcareous shell formed in a corpus fibrosum; the ovary was otherwise normal, save for dense adhesions to the greatly inflamed tube.

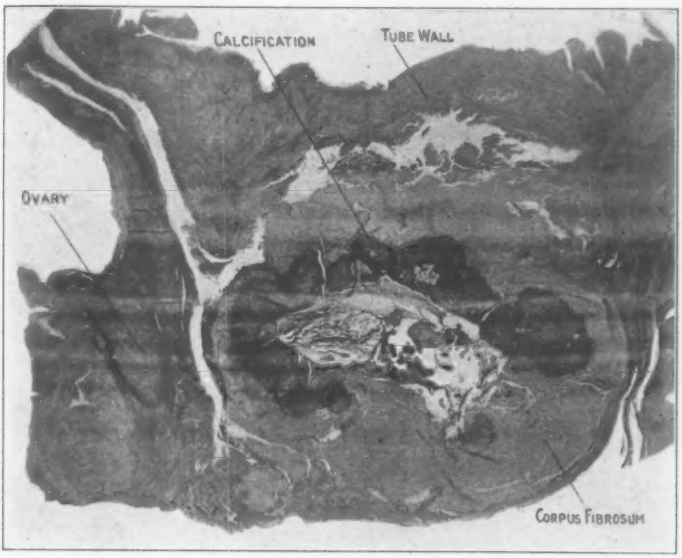

FIG. 2.—Case II. Low-power photograph showing calcareous shell formed within a large corpus fibrosum. (The areas of bone in this section are too small to be distinguishable at this magnification.)

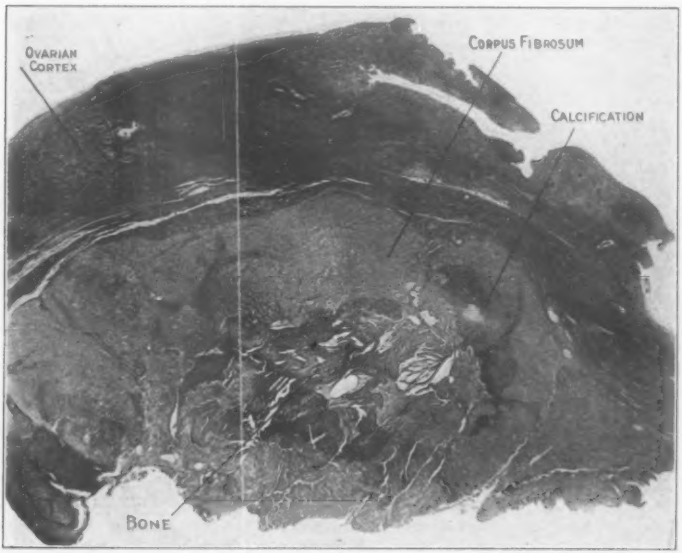

FIG. 3.—Case II. Low-power photograph of a section from a different block of tissue, showing an extensive area of bone in the centre of the corpus fibrosum.

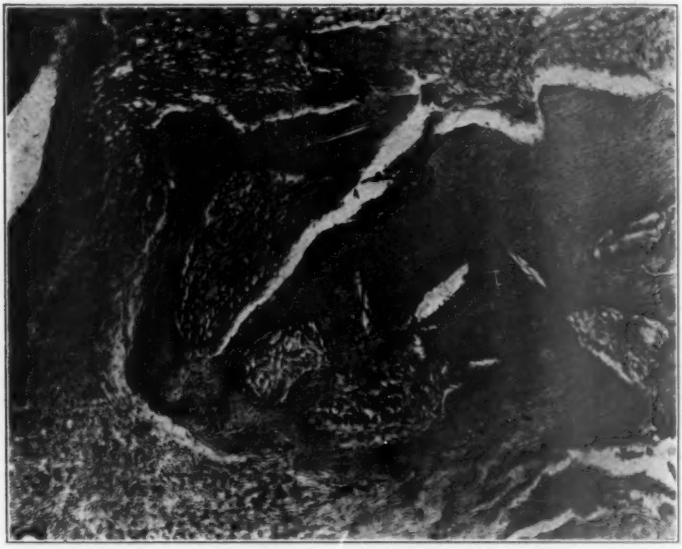

FIG. 4.—Case II. Higher power view of a portion of the bone shown in Fig. 3.

FIG. 5.—Case II. High-power view of another field, showing relationship between fibrous tissue (corpus fibrosum) above, zone of calcification in the middle, and bone below.

CASE III.—Gyn. Hosp., No. 6577. Aged thirty-eight years. *Clinical diagnosis:* bilateral pyosalpinx. *Operation* (Feb. 25, 1913): bilateral salpingectomy; left oöphorectomy; suspension of right ovary. The left adnexa formed an inflammatory, partially cystic mass, which ruptured during removal, permitting the escape of a considerable quantity of pus; drainage. *Specimen:* both tubes; left ovary; small hard nodule. The right tube forms a typical retort-shaped pyosalpinx 11 cm. in length; the fimbriæ are not completely agglutinated, however, and the abdominal extremity is slightly patulous. The left tube forms an indefinite inflammatory mass about 6 x 4 x 3 cm., buried in dense adhesions. The *left ovary* is represented by a mass of torn tissue measuring 5 x 4 x 2.5 cm., which has apparently formed the wall of a cyst or abscess cavity. Accompanying it is a small nubbin of bony hardness, about 2 cm. in diameter, which was shelled out from the left ovary. *Microscopically,* both tubes show intense inflammatory changes. The left ovary (soft portion) shows intense infiltration of the stroma by small round cells. There is one good-sized cyst, apparently of follicular origin. A section through the hard nodule shows the characteristic structure of a corpus fibrosum, with here and there small bits of ovarian stroma about the edge. Throughout the fibrous tissue are extensive areas of calcification, in most of which there is no evidence of bone formation. At one point, however, near the centre of the section, there is a small but distinct mass of true bone, having an irregular outline sharply defining it from the surrounding fibrous tissue, and presenting a similar structure to that of the preceding specimens.

Summary. This case presents an example of a small amount of ossification, occurring in conjunction with extensive calcification of a corpus fibrosum in an ovary the seat of acute inflammation, and associated with purulent processes in each tube.

CASE IV.—U. Pa., No. 3880. Aged thirty-four years. *Clinical diagnosis:* multiple fibroid tumors; bilateral hydrosalpinx. *Operation* (March 25, 1914): supravaginal hysterectomy; bilateral salpingoöphorectomy; appendectomy. *Specimen:* myomatous uterus; tubes; ovaries; appendix. Each tube has been transformed into a typical hydrosalpinx, showing microscopically very active and extensive inflammatory changes. The right ovary is buried in adhesions, but is otherwise grossly and histologically normal. The *left ovary* measures 3.5 x 3.5 x 2.5 cm. Its surface is everywhere covered by adhesions; it is slightly cystic, and at one point contains a small bit of hard, bone-like tissue, less than 1 cm. in diameter. *Microscopically,* the left ovary shows a good-sized serous pseudocyst on the surface and a smaller Graafian follicle cyst within its substance. For the rest, the ovary is histologically normal, the cortical tissue being well developed and containing a moderate number of primordial follicles. Scattered throughout

are about the usual number of corpora fibrosa, in the largest of which are seen a few small, irregular plaques of bone (Figs. 6, 7,

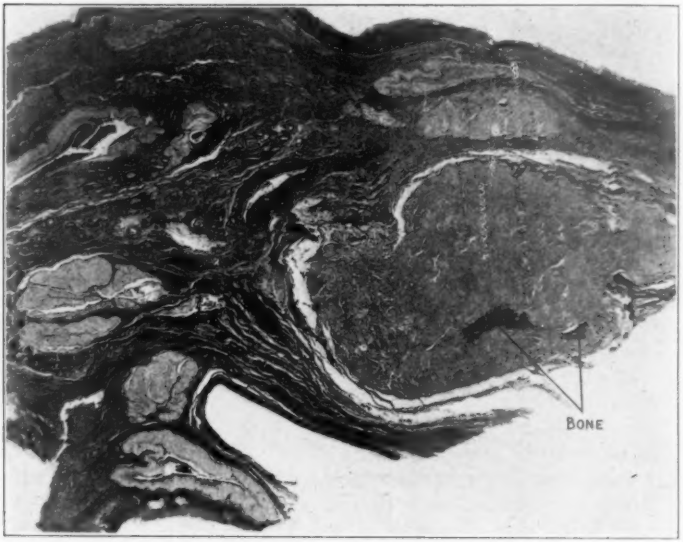

FIG. 6.—Case IV. Low-power view of section through entire ovary, showing numerous corpora fibrosa, in the largest of which are two small areas of bone.

FIG. 7.—Case IV. Higher power view of one of the bone areas shown in Fig. 6.

and 8). These lie within the substance of the fibrous tissue or along its edge. They present the same general characteristics as the specimens described above. The bone is arranged in somewhat irregular lamellæ, scattered unevenly throughout which are numerous small lacunæ, each containing a single deeply staining cell. True Haversian system formation can not be definitely distinguished, but here and there are good-sized cavities, each containing a small capillary bloodvessel surrounded by very loose connective-tissue, presenting an appearance very similar to that of ordinary marrow. The bony areas present everywhere an extremely irregular, dentated edge. There are no evidences in this specimen of a previous focus of calcification, such as are present in Cases II and III.

FIG. 8.—Case IV. Photograph from another block of tissue, showing an area of bone on the edge of the corpus fibrosum.

Summary. This case presents an example of small foci of ossification, apparently without previous calcification, occurring in a corpus fibrosum in an ovary otherwise normal save for the presence of small retention cysts, but associated with old pelvic inflammatory disease.

CASE V.—U. Pa., No. 3893. Aged sixty-eight years. *Clinical diagnosis:* Carcinoma corporis uteri. *Operation* (April 2, 1914): panhysterectomy; bilateral salpingo-oöphorectomy. *Specimen:* uterus;

tubes; ovaries. The uterus, including cervix, measures 8 x 6.5 x 4 cm. It contains a small fibroid; the endometrium is greatly thickened, and presents histologically the characteristic picture of advanced adenocarcinoma, with extensive involvement of the muscularis. The tubes show grossly and microscopically moderate inflammatory changes. The right ovary is represented merely by torn remains of a thin-walled cystic sac. The *left ovary* forms a roughly spherical cyst, about 4.5 cm. in diameter, which has been ruptured. The surface is everywhere covered with adhesions. The cyst wall is for the most part thin and delicate, but in one area is considerably thickened, presenting on the inner surface of this portion several whitish, nodular elevations of almost bony hardness. *Microscopically*, sections from both ovaries show a distinctly fibrous ovarian stroma, containing numerous small cystic spaces lined with a single layer of columnar epithelium, and suggesting on first sight a metastatic invasion from the uterine cancer, but on closer examination the lining epithelium is seen to be so regular, and to show so little tendency to active proliferation, that these formations must be considered probably merely cystic ingrowths from the surface epithelium of the ovary. For the rest, the ovarian stroma appears normal, with numerous developing follicles and corpora fibrosa. The cyst cavity has lost its lining epithelium; it presents the typical appearance of a retention cyst of inflammatory origin. Section through the hard masses shows a loose fibrous stroma, with at one point a good-sized developing Graafian follicle. The major portion of the section consists of very numerous irregular trabeculæ of bone, presenting an appearance practically identical with that shown in Figs. 4 and 13, and having in the interstices a soft, marrow-like tissue similar to that shown in the latter. The Haversian system formation is rather more distinct in this specimen than in any of the others.

Summary. This case presents an example of extensive ossification in a somewhat cystic ovary, associated with pelvic inflammation and an adenocarcinoma of the uterus.

Case VI.—U. Pa., No. 4117. Aged fifty-three years. *Clinical diagnosis:* ovarian cyst. *Operation* (Oct. 31, 1914): Right oöphorectomy. *Specimen: right cystic ovary*, measuring 30 cm. in diameter. The external surface is pinkish white, smooth in places, covered with fibrous adhesions in others. On section the cyst is seen to be unilocular and filled with yellowish, slightly glairy fluid. The cyst wall is for the most part about 2 to 3 mm. in thickness, but at one point there is a hard nodule measuring about 4 x 3 cm. in area by 1.5 cm. in thickness, projecting slightly above the general surface externally, but much more markedly on the internal aspect of the cyst, where it forms a distinct protuberance into the cyst cavity. It presents here the general appearance of being the site of old scar tissue which has undergone considerable contraction, several folds

or plicæ of the cyst wall extending outward from it in a radial manner. It is covered with the same smooth tissue lining the entire

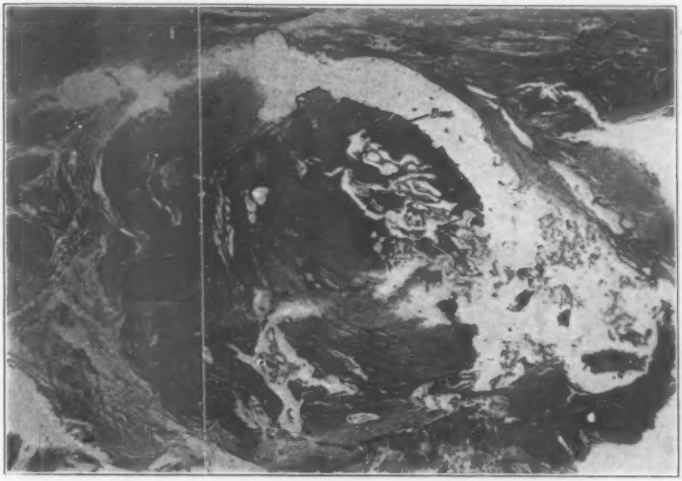

FIG. 9.—Case VI. Low-power photograph of calcified nodule, containing an area of true bone, in the wall of an ovarian cyst.

FIG. 10.—Case VI. Higher power view of the area of bone.

cyst cavity, and there is nowhere any evidence of skin, hair, sebaceous matter, or other dermoid constituents. The nodule is

so hard that it can be cut only with a saw. *Microscopically*, sections from the soft portions show the cyst wall to be composed of parallel, wavy bundles of fibrous tissue containing numerous bloodvessels. At one point a somewhat flattened-out cystic follicle is seen. The main cyst cavity is lined by a single layer of low columnar to cuboidal epithelium, such as is characteristic of the serous cystadenoma. Sections through the hard nodule all show extensive arens of calcification throughout the fibrous tissue, which is here distinctly denser and more hyaline in character than in the preceding sections, with here and there good-sized irregular masses of bone (Figs. 9 and 10). The latter has apparently been formed in close relation to the areas of calcification and secondarily to this process. For the most part this bone, which is quite compact, is present in the form of a central plug or lining inside the calcareous shell, exactly as in Case II; but here and there good-sized trabeculæ of bone extend out through the surrounding fibrous tissue, with which they are in intimate relation, without any intervening zone of calcification.

Summary. This case presents an example of extensive calcification and ossification in one portion of the wall of a cystadenoma serosum of the ovary.

Case VII.—Methodist Hosp. Aged twenty-two years. *Clinical diagnosis:* retroversion; pelvic inflammatory disease. *Operation* (July 10, 1914): dilatation and curetment; amputation of cervix; appendectomy; suspension of left ovary; removal of hard nodule from Douglas's pouch. This case presents some features of unusual interest. On opening the abdomen the uterus was found to be normal in size and somewhat retroverted; there were a few delicate adhesions in the pelvis, which were broken up without difficulty; the left tube and ovary were normal, but the right adnexa could not be located. The right uterine cornu ended in a little nubbin of tissue, not more than 0.5 cm. in length, apparently corresponding to the stump of the tube, but beyond this no trace of that organ was present, nor were there such dense adhesions in this region that there was any possibility of the tube remaining unrecognized among them. The ovary, likewise, was lacking from its normal situation, and nothing corresponding to it could at first be discovered; but on inserting the hand well down into Douglas's pouch, this was found to be occupied by a tag of omentum, embedded in which was a little stony nodule. It was at first thought that this might be an unusually large phlebolith, although this would be a rather uncommon situation for such a formation; but on more thorough exposure it was seen to be just about the size and shape of a normal or slightly shrunken ovary. It was removed simply by shelling it out from the omental tissue. *Specimen:* an almond-shaped mass, measuring 2.5 x 1.5 x 1 cm., of bony hardness, having a somewhat wrinkled external surface. No soft tissue whatever was

discernible grossly, the nodule presenting the appearance merely of a bit of dense bone or calcareous material. It was sawed in half longitudinally, and on section presented the same solid appearance. Decalcification was tedious, requiring many weeks, but finally it was possible to embed the tissue and cut microscopic sections.

Microscopically, a longitudinal section through the entire specimen (Fig. 11) shows the following characteristics: Externally there is a narrow ring of fibrous tissue, arranged in more or less parallel bundles, and containing numerous small bloodvessels and many minute foci of calcification. Here and there bits of fat are adherent to the external surface. For the most part this zone of fibrous

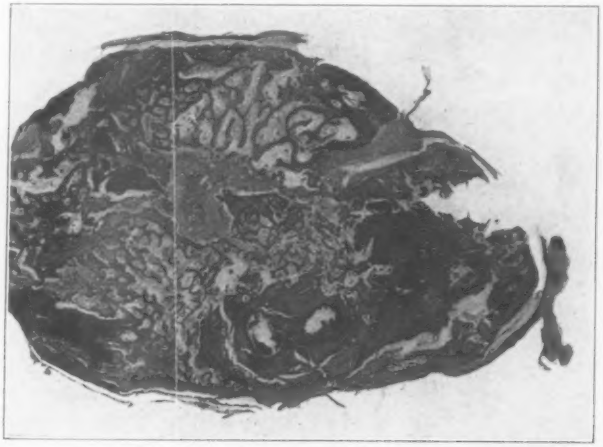

FIG. 11.—Case VII. Very low-power view of a longitudinal section through the entire specimen. The fibrous capsule is seen about the periphery, somewhat mutilated. The grayish areas in the cortex, especially near the right end of the section, correspond to the degenerated tissue mentioned in the description. The bony trabeculæ constituting the major portion of the specimen are well shown. The pale area in the centre is loose fibrous tissue.

tissue remains exceedingly narrow, but in one or two places it dips down somewhat into the interior, being here distinctly looser in structure than on the periphery. By far the major portion of the specimen within the fibrous capsule, however, is made up of multitudinous bony trabeculæ, the whole greatly resembling a section through a piece of ordinary spongy bone. The trabeculæ are fairly thick in the cortical region, forming here good-sized solid masses of bony tissue (Fig. 12); but as the centre is approached they become thinner and more delicate (Fig. 13). The interstices between them are filled with an exceedingly loose areolar tissue, presenting practically the appearance of ordinary marrow, and containing many fat cells, numerous small capillary vessels, and here and there

areas of small round-cell infiltration. In addition to these types of tissue there are several large areas of granular material, taking in hematoxylon-eosin preparations a dull bluish stain, and apparently representing greatly degenerated stroma tissue; throughout these a few small foci of calcification are seen. Some of these degenerated areas are completely structureless, while in others the more or less vague outlines of numerous small bloodvessels can be made out, together with many brownish pigmented cells, such as are often seen in the neighborhood of degenerated corpora lutea. In one of the largest of these areas there are a couple of large,

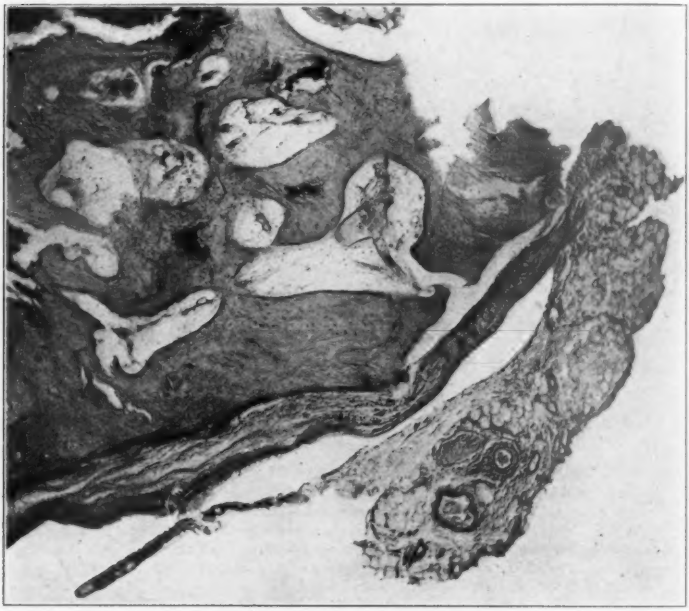

FIG. 12.—Case VII. Higher power view of a portion of the cortex, showing fibrous capsule, with bit of adherent fatty tissue, and thick trabeculæ of bone.

irregular cavities, with ragged edges and masses of apparently cellular detritus in the centre; the general appearance of these suggests that they may very probably represent the remains of somewhat cystic follicles, but the tissue is so degenerated that it is impossible to determine this with certainty. It is evident that the extensive degeneration of this tissue must have taken place *intra vitam* and not merely as a result of the long sojourn of the specimen in the decalcifying fluid, since the outer zone of fibrous tissue, the fat adherent to it, and the medullary tissue throughout the specimen are all exceedingly well preserved.

Summary. This case presents an example of complete atrophy of the right tube, with absence of the right ovary from its normal situation, this structure being apparently represented by an almost completely ossified mass of tissue attached to a tag of omentum deep down in Douglas's pouch.

On account of the almost complete ossification of the little nodule in this case, together with the degeneration of the few areas of soft tissue remaining, it can not, it must be admitted, be identified with absolute certainty as ovary. In view, however, of the entire absence of anything else corresponding to the ovary on

FIG. 13.—Case VII. High-power view of the more delicate bony trabeculæ from the central portion of the specimen; showing also medullary tissue between them.

the right side, with the associated atrophy of the tube, and in consideration of the form, size, location, and at least suggestive microscopic findings detailed above, by far the most plausible explanation for this little bony nodule would seem to be that it represents the remains of the right ovary, which has undergone a spontaneous separation from its normal attachments, with secondary degenerative changes. This opinion finds considerable support from a study of the literature, in which reports of a number of more or less similar cases are to be found. The occurrence of partial or complete atrophy of the adnexa of one side, associated with a normal uterus and opposite adnexa, has been noted from

time to time, but until the first fairly comprehensive study of the subject by Rokitansky, in 1860, such cases were always considered due to developmental anomalies. Rokitansky reported 15 cases in which some degree of atrophy had occurred, usually associated with detachment of the adnexa from their normal relations, and showed that definite pathological processes, occurring either during intra- or extra-uterine life, but *subsequent* to the primary formation of the organs in question, may be responsible for this condition.

Since that time quite a few writers have interested themselves in this subject, and our knowledge of it has been enriched by numerous reports of cases. In the chapter on Diseases of the Ovary in Veit's *Handbuch*, 2d ed., Pfannenstiel says that in cases of this sort "both organs (tube and ovary) are usually lacking from their normal situation, or only the ovary may be entirely absent; if present at all, however, the latter is usually at least atrophic, shrunken, or otherwise pathologically altered. It is often found to have formed an anomalous attachment somewhere in the abdomen; for instance, to the omentum, on the pelvic brim, in Douglas's pouch, or on the urinary bladder. Under these circumstances it is usually greatly shrunken, necrotic, and at times calcified, or transformed into a sac filled with old blood clot." Frankl, in his recently published *Pathological Anatomy and Histology of the Female Genital Organs*, declares that "cases of complete amputation of the ovary, which then lies as a shrunken mass in Douglas's pouch, are not exceedingly rare," and in a paper published last year, Ogórek was able to collect nearly a hundred examples of spontaneous amputation of the uterine adnexa from their normal attachments. After careful consideration of all features of the question, Ogórek, in common with most modern authorities, has come to the conclusion that such separation may occur in only two ways: either as the result of (1) *torsion*, or (2) *strangulation by inflammatory peritoneal bands*, the former occurring when free mobility of the adnexa exists, the latter when these organs are more or less fixed by adhesions to surrounding structures. Once such separation has taken place, he says, the bit of tube left attached to the uterus shrinks to a small nubbin, whose appearance is identical with that of the stump often left after a salpingectomy. The detached distal portion of the tube in many instances undergoes necrotic changes and is absorbed; in others it may remain as an unrecognizable tissue mass somewhere in the pelvis, or may even wander into some distant portion of the abdomen.

The first of these conditions—*i. e.*, a small nubbin of tube at the uterine cornu, with complete absence of the remainder—is exactly that which was present in the case under discussion. In place of the ovary at its normal situation, the oval mass of bony tissue described above was found attached to the omentum deep down in

Douglas's pouch. It is easy to comprehend that following a spontaneous amputation of the right adnexa, whether due to torsion or strangulation, but probably the latter, the ovary in this instance, instead of undergoing necrosis and complete disappearance like the tube, formed new attachments to the omental tissue. With the great disturbances in its nutrition that must have followed, however, degeneration, calcification, and finally ossification were not unnatural sequelæ, and no doubt represent the actual sequence of events. While I have not been able to find any record of an exactly parallel case of histologically demonstrated *ossification* of a spontaneously amputated ovary, it seems most probable that such would have been brought to light had more careful studies of such organs been made. Rokitansky, indeed, in his paper of 1860, speaks of several cases in which the detached or twisted ovary showed a calcareous or bony consistency; but it is evident from his descriptions that at least some of these were dermoids, and, at any rate, pathological knowledge was too undeveloped at that time to make his opinion on this point of value. In the more recent literature at least two cases have been reported which present striking points of similarity to the one under discussion; both these are described by their authors as cases of *calcification* of the ovary, but as no microscopic examination was made in either instance, the possibility that in reality ossification may have been present can not be excluded. These cases are briefly as follows:

Prince (1895). "Miss B., aged forty years; examination revealed a uterus studded with small fibroids. . . . On passing my fingers (at operation) over the posterior surface of the uterus they came in contact with a hard body, loosely adherent, and easily separated from its attachments to the uterus. The right ovary was present and cystic. This with the tube was removed. The left ovary and tube were absent; all that remained was a short stump of the tube about one-fourth inch long. On examining the hard body removed from the posterior surface of the uterus it was found to be the exact size and shape of the ovary. It was free in the pelvic cavity save for the very slight attachment to the uterus by its rough surface. The ovary must have attained full size in its normal position, when for some cause it became detached with the tube, probably from some constricting agency, which has done a neater amputation than could have been done by any surgeon. All vestige of any constricting band, or of the amputated tube, had disappeared."

Miländer (1903). The patient was aged twenty-one years; a nullipara. A large cyst with twisted pedicle was present on the right side; "the left broad ligament was very delicate, the left tube very thin, and its distal extremity not to be found. On careful examination a flat, almond-shaped body was found on the left side in Douglas's pouch, with its long axis transverse, lying free on

the peritoneum, from which it was removed with forceps. This free body was found to be the calcified left ovary; in places it was of stony hardness, in others less dense. It measured 2.8 x 1.6 x 0.8 cm.; the surface was rough and irregular. On section various small, hard masses could be lifted out with forceps, evidently calcified corpora lutea." The author suggests that the calcification was due to disturbances in nutrition caused by pressure of the cyst on the opposite side.

Returning to the question of ossification of normally situated ovaries, there are, as has been said, surprisingly few cases on record. Those mentioned by Pozzi and Bender, in addition to their own, were reported by Fürst, Pfannenstiel, Schroeder, Strauch, and Waldeyer. In going through the literature, I have come across the following additional instances, the essential features of which are here given as briefly as possible:

Winckel (1886). A completely ossified ovary, the size of an adult head, measuring 40 x 40 x 15 cm.; the interior cystic, the cyst wall of bony hardness, showing in thin sections (ground, not decalcified) typical lamellæ and bone bodies.

Coe (1892). One ovary the seat of cystic degeneration, the other of chronic ovaritis; the latter contained a small, hard nodule, which microscopic examination showed to be true bone. Centre of nodule gelatinous, consisting of bone marrow. No evidences of dermoid.

Copeland (1892). Hard growth in each ovary, so dense that it was almost impossible to cut through them with a jeweler's saw. A thin piece secured by grinding presented the histological appearance of longitudinally cut bone.

While the presence of true bone in these cases of Coe and Copeland appears to have been fairly well confirmed by microscopic examination, Williams (1893) contended that both were merely examples of calcification, and expressed his belief that "it is very doubtful if true ossification occurs, although a few apparent cases have been reported."

Robertson (1912). Right ovary 12.5 x 15 cm., of bony hardness. When sawed through, found to consist of a solid wall with a cavity in the centre filled with grayish material. A section of the bony mass made by grinding a thin fragment on a water stone showed atypical bony tissue with irregular spaces and canals; no typical Haversian systems; no evidences of teratoma. The author thinks the bone represents a metaplasia of fibrous tissue.

Moschowitz (1913; 2 cases). Case I.—Double salpingo-oöphorectomy for tubal tuberculosis. In the right ovary a dense nodule having a convoluted surface. On section "the outer third of this nodule was found to be composed of lime salts with many cavities, around which conversion into true bone is taking place. The central portion of the mass consists of true bone, with lamellæ,

bone cells, and Haversian canals containing well-formed bloodvessels, fibrous tissue, and fat. The ossification is evidently spreading eccentrically." Case II.—Hard mass the size of a pecan in centre of ovary. Findings similar to those in Case I, but more advanced.

Adachi (1913). Left ovary measures 2 x 1.5 x 1 cm. At one edge a somewhat hard mass palpable; after decalcification easily recognized as a corpus albicans, with an area of calcification and irregular trabeculæ of well-formed, compact bone, containing spaces evidently marrow cavities, and Haversian canals. In the marrow tissue connective-tissue cells, myeloblasts, myelocytes, plasma cells, lymphocytes, erythrocytes, etc.; no osteoblasts. Bony tissue is in central portion of the area of calcification.

In addition to the above-mentioned cases it is of course possible that other instances may be scattered through the literature, but in view of the fact that I have been able to collect from a moderate amount of pathological material no less than 7 additional ones in a comparatively short space of time (all but one of these occurring within two years), it certainly seems that the condition must be far more common than might be assumed from a study of the literature.

The question naturally arises as to the origin of the bone in cases of this type. The first thought might be that it is always a teratomatous manifestation, in view of the frequent occurrence of such tumors in the female sexual glands and of their well-known tendency to produce bony tissue. Even in cases such as those reported in the present communication, where careful microscopic examination has failed to reveal the least indication of other abnormal tissues, the argument might be advanced that we are here dealing with examples of the so-called "reduced" teratoma, in which it may be assumed that all varieties of tissue save one have been suppressed, as is believed to be the case in certain thyroid-like and other anomalous growths of the ovary. This theory I have discussed at some length in a previous paper, and do not therefore wish to enlarge upon it here. Suffice it to say that while this hypothesis has many points in its favor in the case of growths consisting of highly organized glandular tissue, such as thyroid, a much simpler and more plausible explanation for the occurrence of bone in the ovary would appear to be that it arises as a result of metaplastic changes in the fibrous tissue with which that organ is so well supplied. The tendency of old fibrous tissue, especially if the seat of chronic inflammatory processes, to undergo calcification is of course well known. The occurrence of true ossification in such areas is also a matter of frequent observation, and, indeed, abnormal ossification has been noted in almost all parts of the body, especially the muscular system, bloodvessels, old scars, etc., and cases have been reported involving the kidney, penis, thyroid,

pleura, lymph glands, and various other organs.[2] In several of the cases considered in the present paper the ossification was located in the substance of a corpus fibrosum, *i. e.*, in an area of more or less inert, avascular fibrous tissue; in others, in the fibrous tissue of a cyst wall, or in an atrophic, degenerated organ. In a number of cases the ovary affected was associated with a chronic pelvic inflammatory process of high grade. In almost all instances the ossification was evidently secondary to more or less extensive calcareous deposits in the fibrous tissue, and in the instance where this was most markedly absent (Case IV) the ovary was otherwise wholly normal, save for perioöphoritic adhesions, and in no way suggested the existence of a teratomatous neoplasm.

In addition to the above arguments it may be mentioned that most authors who have interested themselves in this subject have likewise arrived at the conclusion that the bone is purely metaplastic in origin rather than neoplastic. The best term to apply to the condition would therefore appear to be "ossificatio ovarii" rather than "osteoma," notwithstanding the use of the latter by Pfannenstiel and one or two others.

CONCLUSIONS. As a result of the study of 14 cases from the literature and of 7 personal observations it appears that true ossification of the ovary may occur independently of any neoplastic or teratomatous process. Such bone formation is probably metaplastic in character; it occurs chiefly in corpora fibrosa or fibrous portions of the stroma, and particularly in ovaries from cases of pelvic inflammation. In one instance of the personal series it involved the wall of a serous cystadenoma, and in one a spontaneously amputated ovary which was found adherent to the omentum at the bottom of Douglas' pouch, associated with complete atrophy of the corresponding tube. It is highly probable that true ossification of the human ovary, of non-teratomatous origin, is far more common than has generally been believed.

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GANGRENE OF THE LUNG FOLLOWING ARTIFICIAL PNEUMOTHORAX.

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Gangrene of the lung in pulmonary tuberculosis is a very rare condition. Gangrene of the compressed lung in a patient treated with artificial pneumothorax is exceedingly rare; in fact, no case, to the writer's knowledge, has thus far been reported in literature. The following is a report of such a case, with autopsy.

The patient was an American, aged forty-one years; single; teacher. His father died of pulmonary tuberculosis, aged sixty-nine years.

The patient had had numerous attacks of gonorrhea many years before.

The present illness began with a cold. This he was unable to throw off, and three months later definite physical signs were found, and there were tubercle bacilli in the sputum. On his way north to Saranac Lake he went to the Johns Hopkins Hospital, where the Wassermann and gonorrhea-fixation tests were found negative. On his arrival at Saranac Lake he was not below normal weight, had considerable cough and expectoration, and an afternoon fever of 100° to 101°. The chest examination showed a hyperresonant note over the left side, fair breathing, and coarse rales over the

entire front. On the right side posteriorly indefinite rales were heard to the seventh vertebral spine. There was a slight scoliosis, with convexity to the right. The rest of the physical examination was negative.

The urine was normal. The sputum contained many tubercle bacilli, and numerous secondary organisms, chiefly streptococcus and staphylococcus.

No special comment is needed here. The case was an ordinary one of advanced active tuberculosis, involving the greater part of the left lung, and a probable involvement of the upper part of the right. The patient was put to bed and a cough sedative given.

During the next two months he did poorly. The cough became very troublesome and the expectoration increased greatly in amount. The temperature ranged daily between 101° and 102°, with morning remissions. The left chest showed dulness and medium coarse rales over most of the side, with signs of cavitation from the clavicle to the fourth rib. The right chest showed fine rales and deep rhonchi to the seventh rib.

The left lung was disintegrating, and the patient was failing rapidly. With the hope of controlling the advancing process in the left lung, artificial pneumothorax was performed. The history of the seven punctures made is as follows:

Entrance was made in the seventh interspace in the anterior axillary line. The pleural cavity was easily found on the first try. The water manometer read -3 to -11; 350 c.c. of warmed nitrogen gas were injected. Pressure was left at -2 to -6. Two days later 500 c.c. were injected, the pressure being -36 to -9 before and $+2$ to -1 after the injection. Four days later on entrance the manometer read -3 to -8. About 500 c.c. had flowed in when the patient suddenly gave a sharp cry and seized his side near the needle entrance. He held his breath for a moment and groaned as if in great pain. The pain quickly passed off. The pressure was $+2$ to -2. This was watched for a few moments, but there were no changes. Apparently there were no ill-effects from this refill.

A week later on entrance the manometer read $+3$ to -3. This increased pressure was doubtless caused by the presence of a small amount of fluid. At the next operation, the pressure being -3 to -10, 400 c.c. of gas were given and the pressure left at $+2$ to -2.

Meanwhile there had been no noticeable abatement in the symptoms. Although the patient said he felt much better his cough was very hard and explosive, the expectoration was increased, and the temperature persisted. Breath sounds being heard over the upper part of the left chest it was decided to put a greater pressure upon the lung. Accordingly 800 c.c. were given, the pressure being -5 to -10 before and $+6$ to $+2$ after the operation. The patient had no distress although feeling "tight," a sensation that lasted but a few hours.

Two weeks later the fluid was as high as the seventh rib. To satisfy the patient, 200 c.c. of gas were injected and pressure left at +5 to 0. At entrance the manometer showed +1 to −4.

This is the record of the nitrogen injections. It is to be noted that except for the sudden pain during the third operation (considered as a torn adhesion) there was nothing untoward in signs or symptoms caused by the treatment. A small amount of fluid formed, but this is encountered in the majority of cases. The pressures were moderate. The amounts of gas taken were small, but from the signs and symptoms it was judged that the collapse was not complete, and fluid was present which at no time was great enough to be withdrawn.

The patient was too ill to have Roentgen-ray pictures taken. The chest examination, besides the fluid, showed diminished and absent breath sounds over most of the left chest except at the apex and along the vertebral groove. The signs in the right chest remained the same.

His symptoms continued without abatement and his general condition became progressively worse. One afternoon, nine days after the last injection of gas, he suddenly raised a large amount of exceedingly foul, greenish sputa. The next morning, during a coughing spell, he filled five or six sputum boxes with the same putrid matter. He said that it burnt his mouth like fire. The stench was noticeable throughout the house. For nearly three weeks this state of affairs continued. He used about two boxes a day. At times the intensity of the odor diminished. On three occasions he raised from a half to one ounce of blood. Toward the end the expectoration became chocolate colored and watery.

The sputa examined showed mostly pus, enormous numbers of acid-fast bacilli, and also Oïdium albicans, Staphylococcus pyogenes aureus, and a Gram-negative bacillus which produced gas smelling like methane.

No breath sounds were heard on the left side. A metallic tinkle was present. A moderate amount of fluid was made out. There were a few scattered rales on the right side.

The patient sank lower and lower, and finally died three weeks after the first evidence of gangrene of the lung.

Autopsy. Aside from a few scattered fresh tubercles on the surface of the liver and slightly enlarged and partly caseous mesenteric glands, there was nothing abnormal found on the examination of the body except the thorax, where the findings were as follows:

On opening the thorax the heart is found pushed over almost to the midline. The left lung is collapsed and lies against the vertebral column and mediastinum. The pleural cavity contains about one liter of brown, foul-smelling fluid. The collapsed lung occupies about one-third of the left thoracic cavity, being 20 x 9 cm. The division line between the lobes is obliterated. The lung is gray

green in color and "mushy." There are adhesions running upward and outward from the apex to the parieties. One adhesion is as large as a finger, and of solid fibrous tissue. The other is small and strand-like. The apex of the lung is very adherent. The base of the lung is bound down to the diaphragm by tremendous adhesions. The lung shows five large cavities opening directly into the pleural cavity. They range in size from 1 x 2 cm. to 7 x 4 cm. Four of these openings occupy the anterior surface of the lung while the fifth and largest is located at the posterior fissure between the lung and parietal pleura The edges of these holes are bevelled and shreds of gangrenous lung tissue are protruding from them. On the parietal pleura, corresponding to the edge of the hole at that place, is a cicatrized ridge as if lung tissue had been torn from visceral pleura which had become adherent to the parietal pleura.

The parietal pleura is 2 to 3 mm. thick. The pleura covering the lung is very dense. Both pleuræ are grayish green in color and covered with slimy exudate.

In removing this lung the parietal pleura was removed also. The lung tissue seen through the various openings is everywhere the same, being composed of grayish green, sponge-like tissue, all evidences of normal lung tissue being destroyed. A section through the apex shows no cavity, but the tissue is more or less solid and mottled and areas of caseation are present.

The right or uncollapsed lung is voluminous. The color is bluish pink. There is a fine adhesion at the apex. Over the posterior portion of the lower lobe the pleura is roughened and lusterless. There is no fluid in the pleural cavity. The middle lobe in its central and lower portions shows dense tuberculous areas. On section, scattered tubercles are seen throughout the upper and lower lobes, averaging 1 to 2 cm. in diameter.

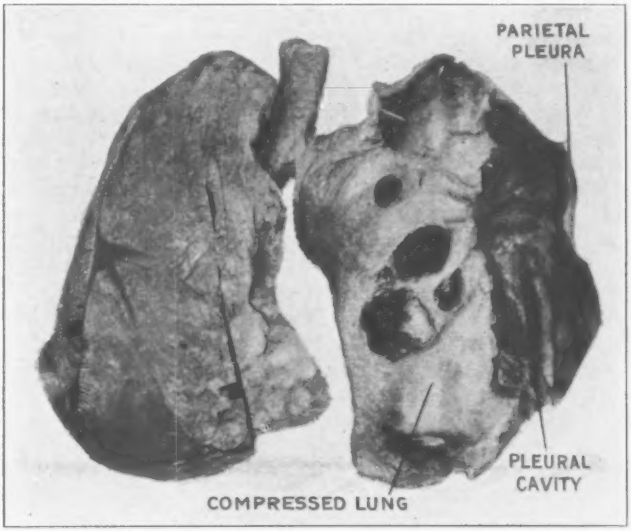
The tracheobronchial glands are grayish black in appearance and moderately enlarged, but do not in any way block or narrow the bronchi by pressure. There is no occlusion of the bronchi or blood-vessels entering the lungs.

Microscopic Examination. A section taken from the apex of the gangrenous lung shows first a greatly thickened pleura composed of dense connective tissue. Scattered throughout the pleura are numerous minute tubercles. Beneath the pleura no normal lung structure is to be seen. There are small slit-like spaces which are compressed alveoli. Distributed throughout are areas of granulation tissue containing small capillaries in which red blood cells are found. In this granulation tissue are also seen fresh tubercles. Dipping down from the pleura is a dense fibrous band. There are also to be seen large tubercles composed of a central area of fibrous tissue and a dense outer ring of round cells. At the edges of the central area are seen giant cells. The bloodvessels show obliterative endarteritis. Throughout this whole layer there is a dense round-cell

infiltration. This layer quickly shades off into an area of non-staining homogeneous tissue in which are scattered portions of nuclei.

Discussion. Was artificial pneumothorax the cause of the gangrene in this case? A brief review of the subject of lung gangrene may help to decide this question.

Gangrene of the lung implies not only death of the tissue but subsequent putrefaction. The necrosis is due to the obstruction of bloodvessels and the deprivation of blood supply. This obstruction may be inflammatory or mechanical. The gangrene is due to the invasion of the necrotic area by putrefactive organisms. Among the



Photograph of lungs showing gangrenous compressed left lung with holes opening into pleural cavity through which may be seen the gangrenous tissue.

organisms found are the pyogenic staphylococcus and streptococcus, the coli communis, and a pseudotubercle bacillus.

A frequent direct cause of gangrene is the retention of putrid secretions within a bronchiectatic cavity; also the inhalation of septic material, either during anesthesia or on account of paralysis of the glottis.

Inflammation of the lungs such as pneumonia may lead to gangrene, although some observers doubt its occurrence. It is interesting to note the rarity of gangrene in pulmonary tuberculosis. One would think that bronchial dilatation, caseous areas, and cavities would offer a good field for its occurrence, yet this complica-

tion is extremely infrequent. But autopsies show that a localized area of gangrene may exist in a lung without producing fetid sputum or breath, as seen in Fox's series, in which 6 cases of gangrene were found out of 100 postmortems in tuberculous subjects. This is a much higher percentage than other authorities have found. Four of the cases had gangrene in pneumonic areas and two on the walls of cavities.

Tumors of the mediastinum may by pressure lead to gangrenous changes; and septic emboli plugging a pulmonary vessel may cause gangrene. In our case the bronchi and root vessels were patent, and no focus was found at autopsy from which septic emboli could arise.

Occasional cases have been reported in which putrid pleural effusions have been withdrawn, and a fistula being established portions of gangrenous lung have been discharged through the opening. These cases coming to autopsy show the lower portion of the lung compressed by the fluid; the fluid is putrid; and the contiguous lung tissue gangrenous. Loculated fetid empyemas tend to burrow through the lung to a bronchus, and on account of the dense adhesions pneumothorax rarely results. Whether these putrid effusions are primary or secondary is often difficult to say. In the case here reported fluid was noticed after the third refill, but there was nothing in signs or symptoms to lead us to believe that it was gangrenous in character.

Bearing more directly is the question whether gangrene follows collapse or compression of the lung by air as in pneumothorax, or by fluid as in pleurisy with effusion. A review of the literature of many years fails to reveal a single case of gangrene of the lung after a natural or artificial pneumothorax. Evidently the entrance of air into the pleural cavity cannot of itself cause gangrene of the lung.

Fox gives pleurisy with effusion as one of the causes of lung gangrene, but cites no cases and doubts if pressure of fluid in the absence of other factors can produce gangrene. I am not aware of any reports illustrating this condition. The nearest approach to it is found in the cases of putrid effusions or empyemas mentioned above.

Whatever the cause of the obstruction the decomposition of retained secretions is believed by Fowler and Godlee to be the main factor in the production of gangrene of the lung.

In the case here reported there were three factors present which, in combination, were probably sufficient to cause the gangrene. They were (*a*) necrotic areas due to obliterative endarteritis; (*b*) pressure of gas and recoil of lung which aided necrosis, and (*c*) putrefactive organisms.

The following sequence of events might have occurred:

1. To begin with there was a rapidly disintergrating lung with superficial cavities.

2. More or less extensive necrosis of lung tissue due to obliterative endarteritis.

3. The introduction of gas collapsed the lung, limiting the blood supply, and thus aiding in the extension of the necrosis.

4. Putrefaction now took place and gangrene supervened upon the necrotic areas.

5. Rupture of the lung then followed and the pleural fluid became putrid and corroding.

Putrefactive organisms and large necrotic areas are frequently present in tuberculous lungs and do not produce gangrene. There is no reason to suppose that had this lung been let alone it would have become gangrenous. It would appear that the collapsing of the lung was the immediate exciter of the subsequent events.

Other lungs in a similar condition have been collapsed without bad results, but evidently such a procedure is fraught with danger.

I am indebted to Dr. Lawrason Brown for the privilege of reporting this case.

REFERENCES.

Wilson Fox. Treatise on Diseases of the Lungs and Pleura, p. 596.
Alexander James. Pleurisy, p. 168 et seq.
Fowler and Godlee. The Diseases of the Lungs, p. 248.

REVIEWS

LEHBUCH DER SPEZIFISCHEN DIAGNOSTIK UND THERAPIE DER TUBERKULOSE F. AERZTE UND STUDIERENDE. Von Dr. PANDALIER, Chefarzt des Sanatoriums Schwarzwaldheim in Schömberg bei Wildbad, und Prof. Dr. ROEPKE, Chefarzt der Eisenbannheilstätte Stadtwald in Melsungen bei Kassel. Achte Auflage. Mit einem Vorwort von wirkl. Geh. rat Prof. Dr. R. Koch, Exzellenz. Seite 409. Mit 25 Temperaturkurven auf 7 lithographischen Tafeln, 2 farb. lith. Tafeln und 6 Textabbildungen. Würzburg: Verlag von Curt Kabitzsch.

THE eighth edition of this work undertakes to bring up to date the efforts of previous editions, and to present as far as possible in one volume the various aspects of tuberculin in diagnosis and treatment. The simplicity and clearness in the arrangement of the different subjects is admirable. The references exceed four hundred in number, and are nearly all to German publications.

With all their enthusiasm for tuberculin in diagnosis and treatment, an enthusiasm this work would incline one to believe is widespread and increasing throughout Germany, the authors in many respects show a commendable conservatism. The precautions to be observed in the preparation and application of tuberculin, the proper selection of patients, the association of this with all other available methods to combat tuberculosis, and the limitations of tuberculin, are all emphasized and presented with much detail. While not claiming for tuberculin all the efficacy one could wish is actually possessed, they attribute a very high place to it among the various means at our command. Small initial doses are used in treatment, and reactions are avoided or limited. Albumose-free tuberculin is the form most recommended, supplemented, in proper cases, by Bacillen-emulsion, thereby to produce both a toxic and a bacterial immunity. The author's efforts and hopes have lain chiefly in the production of an active immunity.

It would be a great satisfaction to be able to subscribe to all the claims of this work, which is based on so long and extensive an experience. To properly support any other attitude with full justice to either the authors or the reviewer is impossible within a brief space. The burden of proof, however, lies with the authors. It may be requiring a great deal to ask for greater pathological evidence favoring the value of tuberculin, however important such evidence is, but even the clinical evidence furnished by the

authors is not satisfying. From the large sum of figures available from many sources it is difficult to glean more than a small proportion that carry real weight. One looks in vain in the present volume for figures that are properly comparative, that is, dealing with cases divided as nearly as possible into two equivalent groups, observed under similar conditions, treated alike except that one of the groups receives tuberculin treatment, and followed up for a number of years while living as nearly as possible under similar conditions. Only two years have elapsed since the authors began to use albumose-free tuberculin.

Exception is to be taken to the authors' general statement that tuberculin treatment is indicated in the hands of the general practitioner, or may become so by the pursuit of proper courses of instruction, especially when such treatment by him follows an initial course of treatment of the patient in an institution. The average practitioner has yet much to learn about the available methods of diagnosis of tuberculosis, and of its treatment with non-specific methods more than can be acquired within a brief period of time, as many who have sought special instruction about tuberculosis are willing to acknowledge. But even with the proper equipment for treating with tuberculin, would the average practitioner possess the requisite amount of time to safely carry on the treatment?

C. M. M.

PRÉCIS DE CHIRURGIE DE GUERRE. By E. DELORME, Médecin Inspecteur Général de l'Armée, Membre de l'Académie de Médecine, Membre et ancien Président de la Société de Chirurgie, grand officier de la Légion d'Honneur. Pocket-size octavo with flexible binding. Pp. 218. Paris: Masson et Cie.

THIS little book was written hurriedly by Delorme shortly after the outbreak of hostilities. It is based on various observations from recent wars. It consists of twenty-one short chapters in which are described weapons and projectiles, wounds of various tissues, and wounds of various regions, from the skull to the feet; while at the end of the book is a series of specimen charts for recording certain data. It is characterized by brevity and clearness.

Most of the book is a record of first, what tissues do to bullets, and second, what bullets do to tissues: one can find out what a bullet is liable to do to practically every portion of the body. The burning, practical questions of the military surgeon when confronted with a wounded soldier are: What has the bullet done, and what is the best thing for me to do? Working in the field hospital under strenuous conditions the surgeon must rely upon his knowledge of anatomy to find out what the bullet did, and upon his "horse sense"

and judgment to determine what is best for the patient. War surgery differs from civil surgery only in the field; from the base hospital rearward there is no difference. With few exceptions conservatism is the thing in the field; the important question to decide is, How far may the patient be transported with safety?

The statement of MacCormac that "A man wounded in the abdomen dies if operated upon; he lives if let alone," is forcibly supported in the following passage: "In the Transvaal, at Spion Kop, all the wounded, being in a mountainous country, and having necessarily to be transported over very rough ground, succumbed; at Jacobsthal a great many men who were not moved recovered. We have seen quite a series of wounded cured by expectation, the soldiers having been obliged to remain on the field of battle for several days without being able to move from one spot, with nothing to drink or eat."

But little is said about wounds from cold steel; nothing on the value of human blood serum in hemorrhage; while the work antedated, of course, the recent exhaustive observations of Fauntleroy on gas-bacillus infection, as well as the prophylaxis and curative treatment of poison-gas cases.

The book should be of great value if read by one about to enter upon medical military service, for it imparts a good, general working knowledge of military surgery. P. G. S., Jr.

The Johns Hopkins Hospital Reports (Monographs, New Series, No. VII) Venous Thrombosis During Myocardial Insufficiency. By F. J. Sladen, Resident Physician and M. C. Winternitz, Associate Pathologist, The Johns Hopkins Hospital. Pp. 40; 2 figures; 1 colored plate. Baltimore: The Johns Hopkins Press, 1915.

This monograph is an admirable summary and discussion of cases of venous thrombosis occurring during myocardial insufficiency. To forty-eight abstracts of cases published in the literature are added seventeen unpublished cases, observed mostly in the Johns Hopkins Hospital. Several facts of interest are brought out: (1) Extensive venous thrombosis is commoner than has been believed hitherto; (2) is frequently difficult to diagnose; (3) should be suspected whenever the edema of myocardial insufficiency is asymmetrical; (4) occurs more often in females than in males, but at any age; (5) most commonly follows rheumatic mitral disease. It should be remembered, however, that myocardial degeneration was probably also present in most of the cases diagnosed primarily as valvular. As an "irregular pulse" is frequently mentioned in the abstracts, it would be interesting to know whether such types of cardiac

arrhythmia as auricular fibrillation bore any relation to the incidence of thrombosis. From this point of view, the absence of polygraphic or electrocardiographic records is regrettable. It is also unfortunate that in the more recent cases at least, observation on venous blood-pressure could not have been included, as here also a valuable relationship might have been established. Brödel's three illustrations are, of course, excellent. One would appreciate, however, a more detailed description of some of the features of the colored plate. E. B. K.

SURGICAL OPERATIONS WITH LOCAL ANESTHESIA. By ARTHUR E. HERTZLER, A.M., M.D., Ph.D., F.A.C.S., Surgeon to the Halstead Hospital, Kansas, the Swedish Hospital, Kansas City, Mo., and to the General Hospital, Kansas City, Mo. Pp. 132; 173 illustrations. Second edition. New York: Surgery Publication Company, 1916.

IN this the second edition, the author has widened his scope and treated the whole general subject of local anesthesia in surgery. He describes in detail the technic of the injection, the drugs employed, their choice and their administration in minutiæ. Major and minor operations are described and the special method of anesthesia for such is illustrated.

No attempt is made to theorize as to the production of anesthesia. The work is purely a practical one covering this side of the subject from beginning to end. Emphasis is laid upon the knowledge of anatomy and gentleness in all manipulations and surgical procedures.

The book is very well gotten up in every way, the subjects are well arranged, the illustrations well made, clear and instructive, and the text makes very pleasant and easy reading. It tells one all he desires to know about the practical side of local anesthesia. Many apparently minor points, yet very important points are elucidated, points which have been heretofore inexplicable to the reviewer at least. It is a work I am glad to own. E. L. E.

POSTMORTEM EXAMINATIONS. By WILLIAM S. WADSWORTH, M.D., Coroner's Physician of Philadelphia. Pp. 604; 304 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

CRITICISM of Dr. Wadsworth's *Postmortem Examinations* must be favorable or qualified, largely as the book is regarded as a monograph *in extenso* or a text-book for students and practitioners. If offered in the latter sense it is impossible, for it should, as a text-

book, set forth facts and principles commonly accepted among pathologists as proven; or, if not as yet accepted, at least a statement to that effect should be made. Contrary to this the author frequently, and often at length, philosophizes upon personal theories not accepted by the pathological world before being submitted as proper text-book matter. Examples to point are the "gastric hair" and "colds in the kidney." Especially to be deplored is the discouragement of orderly and routine methods in performing postmortems. To one who has performed 4000 autopsies, order may be unnecessary; but to students and occasional obductionists who outnumber the 4000 class 4000 to 1, and for whom the book is supposedly intended, the advice is wrong and rigid adherence thereto unsafe.

Apart from the technical aspect of the book we quote verbatim as follows: "L. died in a hospital of heroin poisoning, and great was the indignation when I pointed to the facial contracture and then cut out an apoplexy" (page 109). And again: "Thirty years ago, while at school, I took pictures, with a sixteen-dollar outfit, that I would be willing to have compared with some that take prizes today" (page 555). An additional space would permit multiplications along similar lines almost *ad lib.* Most certainly the work would make far better reading did not the author go so far out of his way to unnecessarily, uselessly, and indiscriminately "knock" his colleagues (not alone the pathologist, but anatomist, clinician, and general medical literature as well) and keep himself so constantly before the reader. And this applies whether the work be considered as text-book or monograph.

The photographs are uniformly excellent, and by them the author has shown himself the consummate artist and skilled technician; many original devices are shown from time to time indicating real mechanical genius, and the part on medico-legal postmortems brings out many valuable points. But beyond these latter it is difficult to go.

F. S. W.

THE DUCTLESS GLANDULAR DISEASES. By WILHELM FALTA, Vienna. Translated and edited by MILTON K. MEYERS, M.D. Pp. 658; 101 illustrations. Philadelphia: P. Blakiston's Son & Co., 1915.

IF anyone still doubts the truth of the old saying that words were given to man to hide his thoughts, let him borrow the American edition of Falta's work and spend an evening with it.

As a whole the book is a valuable collection of material concerning all phases of the disorders of the ductless glands, and over sixty pages of references to the literature evidence its painstaking preparation. However, our knowledge of the ductless glands today does

not lend itself to finished presentation, and much confusion and contradiction is still inherent to the subject. This complexity is made worse by the author's style, which is unpardonably verbose and discursive, and renders the reading of the book a very doubtful pleasure. Its value to the average reader is uncertain, for it does not pay to work an ore of less than a certain percentage of gold to the ton, and in the reviewer's opinion the gold in the ore in this instance runs perilously low.

But whatever our estimate of the work in the original German, there can be no doubt of its greatly lessened value in the American edition, for in the translating and publishing many further difficulties for the reader have been introduced.

To him, however, who decides to dig in this American edition can be promised some precious gems of careless proofreading. Every few pages the tedious text is enlivened by a sentence the meaning of which has been beclouded by the substitution for the original of a word similar in appearance if not in meaning; thus confer instead of compare (page 89), proves instead of paves (page 51), and placed instead of played (page 36). Similarly can be explained such enlightening statements as: "On account of the marked excretion of sweat, malaria sometimes occur" (page 82), and "The diagnosis made was congenital abscess of the uterus . . ." (p. 438), while the legend to an illustration on page 577 gives a unique translation for "Fettgewebes." It reads, "Inflammatory alteration of the feet-tissue in a case of adipositas dolorosa." Grammar is often ignored and the verb is, as a rule, firmly entrenched at the end of each sentence. The spelling is good except in personal names thus: Hayem is met as Hajem, Morawitz as Morowitz, and C. v. Noorden as C. V. Noorden.

Naturally one's sympathy is aroused for the author whose work has been published for American readers in such a slipshod manner, and one is also a little sorry for the readers, but they at least are free agents, and have the cure for such publications in their own hands.

O. H. P. P.

HYSTERIA AND ACCIDENT COMPENSATION, NATURE OF HYSTERIA AND THE LESION OF THE POST-LITIGATION RESULTS. By FRANCIS X. DERCUM, M.D. Pp. 120. Philadelphia: The Geo. T. Bisel Company, 1916.

THIS short essay on hysteria and accident compensation is apparently intended for the legal profession and as such it presents the subject very well. The author believes that in most instances in which nervous conditions follow accident that the symptoms are largely and in most cases altogether the result of the litigation and that as soon as the litigation is ended all symptoms disappear.

He quotes largely from the German and other literature and from his own very large experience. However, while most neurologists will not agree with this point of view, nevertheless, Dr. Dercum's presentation from this standpoint is a very good one.

T. H. W.

LEGAL PRINCIPLES OF PUBLIC HEALTH. By HENRY BIXBY HEMENWAY, A.M., M.D. Pp. 859. Chicago: Flood.

THIS publication is surely, as is stated in the introduction, a sign and product of the times. We are slowly coming to a realization of the importance of public health work, as is evidenced by the fact that a large percentage of our communities are becoming interested in a manner demanding recognition. The sentiment of the populace, as their education in public health problems advances, is strongly in favor of employing men especially trained in this branch, or, perhaps better, specialty of Medical Science.

The subject matter might be, in some respects, adversly criticized, but the whole work is so excellent that such criticism would seem unwarranted.

The scientific basis of public health work is discussed briefly and clearly. There is one point in this chapter which must be criticized, namely, the interpretation of Koch's postulates. These postulates, as originally formulated by Koch, have been variously modified by different authors, in some instances so greatly that their identity is practically lost.

The different chapters deal with the various phases of the legal aspect of public health questions in as nearly as possible a systematic manner.

The chapters on due process of law and nuisance are followed by public health powers and limitations. After reading and mentally analyzing these three interesting chapters, one is forcibly impressed with the fact that "limitations" are a serious handicap to those who are endeavoring to protect the health of our communities.

The various phases of public health administration are very ably dealt with. Quarantine is considered in some detail. The prevention, legal and commercial aspects are clearly discussed.

The reader is at first impressed with the brevity of the chapter on water supplies, drainage, pure food, and drug regulations; however, on analyzing them carefully, it will be found that the first is excellent, but that the discussion of drug regulations is hardly adequate. It is to be regretted that the work was published before the passage of the Harrison Act.

The last three chapters deal with subjects which are attracting special attention at the present time, namely: industrial regulations, school inspection, and eugenics. Those who have become, as it were, hysterical over the eugenic propaganda, and have carried

their ideas to a point which would lead one to presuppose that they were not themselves absolutely free from mental abnormalities, might well ponder over the last paragraph (512) in the book, which states: The foregoing (*i. e.*, the chapter on eugenics) clearly illustrates that all laws on the subject of eugenics should be based upon the science of biology, no sociologist should attempt to force such legislation without its approval by competent biologists; no legislation is safe upon the subject unless it is reasonable; and to be reasonable it must be grounded on fact, rather than theory; upon science, rather than emotions.

It would seem to the reviewer that this work is an essential in the library of all physicians and officers dealing with public health problems. It contains much valuable information, and the subject matter is treated in such a manner as to make of it exceedingly interesting reading. N. G.

A TEXT-BOOK OF NERVOUS DISEASES, FOR STUDENTS AND PHYSICIANS. By ROBERT BING, M.D. Translation by CHARLES L. ALLEN, M.D. Pp. 481; 111 illustrations. New York: Rebman Company, 1915.

BING's work on nervous diseases is of course very well known and it was a happy thought which led to the translation by Dr. Charles L. Allen, who did his work very well. Instead of the usual method of discussion the author subdivided the subject into lectures. For example in his lecture on multiple sclerosis which is typical, he first gives a definition of the disease, then gives a paragraph in which he discusses the pathology, then a longer discussion on etiology and an ample discussion of the symptoms. After this, the atypical forms of the disease, then the differential diagnosis, prognosis, and lastly treatment. This is the plan adopted throughout the book. As can be seen from this it is the logical manner in which any subject would be presented in a lecture and is different from the usual text-book presentation.

The classifications which the author adopts are very interesting. In dyskinesias he includes all forms of tremor, spasms and coarse movements, even including chorea, athetoid movements, paralysis agitans and myasthenia gravis. From the standpoint of the student this is admirable, but from the pathological point of view, as of course the author would willingly acknowledge, such a classification is not probable. The discussion of the syphilogenic diseases of the central nervous system is excellent and is as good as can be found in any text-book with the exception that the treatment is necessarily just a little out of date inasmuch as the original book was published several years ago. The lecture on arteriosclerosis of nervous centres is the best that the reviewer has read in any book, as is also the chapter on aphasia, apraxia, and agnosis. The

lecture on tumor formations is disappointing in the sense that it is not large enough and leaves a good deal to be desired. The discussion and classification of what Bing terms dysglandular symptom complexes is excellent. He includes in this Basedow's disease, myxedema, Addison's disease, and dyspinealism. His lecture on the sympathetic and trophoneurosis leaves nothing to be desired. The illustrations are excellent and far better than what is found in most text-books on nervous diseases. The diagrams, most of which are taken from his compend, are also excellent. Altogether it is one of the best and most satisfactory works on nervous diseases that has appeared for some time, and is far better than some of the more recent books by American authors. From the point of view of the student it is in the reviewer's mind the best work that has appeared for many years. T. H. W.

SEROLOGY OF NERVOUS AND MENTAL DISEASES. By D. M. KAPLAN, Director of the Clinical and Research Laboratories in Neurological Institute of New York. Pp. 346.

THIS volume confines itself entirely to the serology of nervous and mental diseases and practically to those dependent upon syphilitic infection. It is the first collected study of these reactions appearing in English, and fills a unique place in the library of clinical tests.

Kaplan divides the book into four parts. The first deals with the technic used in collecting blood specimens, making spinal punctures, and with the description of the methods used in the actual performance of the various tests: Wassermann reaction of blood and spinal fluid; gold solution; globulin reactions; spinal-cell counts, and the reduction of Fehling's solution. These tests are so briefly and adequately described that anyone at all familiar with the serological technic could easily follow them. The second part deals with the serological findings in the various mental and nervous diseases using these five tests. Beginning with the diseases of the meninges, he gives the formula in practically every involvement of the central nervous system. The third part confines itself to syphilitic diseases, describing in detail every combination of findings in cerebrospinal syphilis, tabes, and paresis, with the average changes occurring in these formulas under successful treatment. The fourth part deals with the preparation and the technic of administration of salvarsan.

The book fills a real need and as a text-book is equally valuable to the general practitioner, neurologist, and laboratory worker. One can not but regret that it is so definitely limited to syphilis and that some of the other serological tests are not included.

S. D. W. L.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Urochromogen Test in the Urine in Typhoid Fever.—V. SVESTKA (*Wien. klin. Wchnschr.*, 1915, xxviii, 1054) has studied the urochromogen test of Weiss and the diazo test of Ehrlich in a series of cases of typhoid fever. He found both tests positive in all of 52 cases of typhoid fever and 3 of paratyphoid fever. In 26 cases of suspected typhoid, all of which remained negative bacteriologically, each test was positive in one case only. Each test was also positive in only one of 45 healthy individuals vaccinated against typhoid fever. The author performed the test as Pulay described it, except that he diluted the urine till it was colorless; only an intense canary yellow color was looked upon as positive. The urochromogen test was positive in the first week of typhoid fever. The bacteriological diagnosis in the cases studied was positive during the second week.

Anaplasma like Bodies in the Blood of Vertebrates.—ANNIE PORTER (*Ann. Trop. Med. and Parasit.*, 1915, ix, 561) calls attention to the fact that many papers have been written during the past ten years dealing with blood parasites occurring in the blood of vertebrates, and points out that some papers would have been much improved by a careful preliminary study of the elements of apparently normal blood, or of blood under definite pathological conditions. By such a study a number of so-called "parasites" would have been found to be artefacts or reaction products and not true organisms. She particularly calls attention to the fact that this is probably true of the bodies called by Theiler "anaplasmata" and considered by him to be the cause of "gall sickness" in cattle in South Africa. In the present study the

author has examined the blood of a number of vertebrates and has compared them with specimens taken from South African cattle and blood from obscure cases of human anemia. Viewed in the fresh, anaplasmata appear as small rounded granules without morphological differentiation within the erythrocytes. They usually are single, but forms apparently dividing may be seen. They show no differentiated structures by intra-vitam staining. In stained preparations these structures are usually round, rarely irregular and take a deep chromatin or basophilic stain. Forms resembling diplococci are not uncommon. The author comes to the conclusions reached by a number of others, which is to the effect that the so-called "anaplasmata" are not protozoa but that they represent a product of the degeneration of the red cells due to the action of some vital substance or substances in the host. They occur in healthy and anemic vertebrate bloods, both warm and cold blooded. The author is of the opinion that probably these bodies are of nuclear origin.

A Test for Urobilin in Urine and Feces.—A. EDELMANN (*Wien. klin. Wchnschr.*, 1915, xxviii, 978) describes a modification of Schmidt's urobilin test which is applicable to both urine and feces and which is much quicker than the original test. Instead of a saturated aqueous solution of bichloride of mercury he employs a saturated alcoholic solution; the latter contains about twice as much bichloride as to the aqueous solution. The technic for applying the test to the urine is as follows: Two reagents are necessary: (1) a concentrated alcoholic solution of bichloride of mercury; (2) a 10 per cent. alcoholic solution of zinc chloride, and amyl alcohol; about 10 c.c. of urine in a test-tube are treated with half the volume of concentrated alcoholic sublimate solution, mixed, and then shaken with amyl alcohol (which is best accomplished by pouring the contents down the wall of a second test-tube several times.) To the clear amyl alcohol layer which quickly separates above, several cubic centimeters of the alcoholic zinc chloride solution are added; or the amyl alcohol may be poured into another tube and treated with zinc chloride. With large amounts of urobilin the amyl alcohol is saturated with the pigment and shows a beautiful rose red color (only with pathological amounts of urobilin) and the addition of zinc chloride produces an intense green fluorescence. With small amounts of urobilin, if the fluorescence is not visible with diffuse light, the light may be focussed on the tube with a convex lens, or the light from a small electric flash may be employed. By this means traces of urobilin may be detected. In applying this test to the stools, several grams of feces are rubbed in a mortar with a very small amount of water. Then an excess of reagent I is added, and rubbed a minute longer and filtered into a clean test-tube. To the filtrate, which is red in the presence of urobilin, the addition of a few cubic centimeters of solution II causes a green fluorescence.

The Sterilization of Fluids by Means of Animal Charcoal.—R. KRAUS and B. BARBARA (*Wien. klin. Wchnschr.*, 1915, xxviii, 1031) have previously shown that animal charcoal adsorbs typhoid and

cholera bacilli from water, so that the water may be bacteria-free after one hour. Further experiments have shown that this result may be accomplished in a much shorter time. Thus, 100 c.c. of distilled water, 1 gram of animal charcoal + $\frac{1}{10000}$ loop of cholera culture per cubic centimeter were shaken together. After fifteen minutes 1 c.c. of the filtered fluid was placed upon agar plates. After twenty-four hours the plates were sterile. With typhoid bacilli they found it necessary to use three to four times as much charcoal to make the water sterile. They have used this method in an attempt to sterilize milk and found that 100 c.c. of milk bought in the market, when shaken with 3 grams of animal charcoal and allowed to stand fifteen minutes, can be passed through a filter paper and recovered bacteria-free. For the sterilization of serum the method has also proved useful. Anti-agglutinins, for example, are not adsorbed by charcoal, as are toxins. Antidiphtherin serum loses none of its potency when treated in this way, though there is a loss in filtering through bacteriological filters.

Spontaneous Agglutination of the Erythrocytes in Malaria.—R. BIGLIERI (*Wien. klin. Wchnschr.*, 1915, xxviii, 1054) had his attention called to the fact that red blood corpuscles in malarial blood frequently clump on the slide when a preparation is made by the Ross thick drop method. This phenomenon has not been observed with normal blood. Mornaco and Panici have described an agglutination which occurs when the serum from malarial patients is mixed with human corpuscles. French observers have also noted an agglutination of the erythrocytes in patients suffering with trypanosomiasis. The author examined the blood of 600 patients ill with malaria and 158 of the specimens showed agglutination of the red blood corpuscles in the thick drop. This spontaneous agglutination was found with equal frequency in tertian and quartan infections and somewhat oftener in estivo-autumnal. In 54 cases which exhibited symptoms of malaria, in whose blood no parasites could be found, agglutination was also observed. Spontaneous agglutination of the erythrocytes was also found in septicemia and in pregnancy. The cause of the agglutination has not been discovered.

SURGERY

UNDER THE CHARGE OF

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A Simple Operation for Femoral Hernia.—BRUNZEL (*Deutsch. Ztschr. f. Chir.*, 1916, cxxxv, 67) says that, as a rule, the chief obstacle to the complete closure and removal of the femoral canal is the very tense and

rigid overlying Poupart's ligament. The only simple way of overcoming this tension is to divide the ligament. This can be done, without disturbing important anatomical relations, over the iliopsoas muscle. Brunzel first tried this method toward the end of 1914, in a case of strangulated femoral hernia, and since then in over a dozen other cases, some with very large femoral herniæ and all with good results. An incision along Poupart's ligament gives a free exposure of the parts and permits a certain diagnosis between an inguinal and femoral hernia and the opportunity of operating on whichever is found. The sac of the femoral hernia is isolated, opened, its contents reduced, the sac ligated at its neck and cut away. The stump is pushed upward into the abdomen by the finger and the femoral canal freed of fat. A vertical incision is now made through the aponeurosis of the external oblique, including its lower border or Poupart's ligament, over the iliopsoas muscle. Poupart's ligament can then be pressed inward at the site of the femoral canal, when it will hold this position almost without further aid. A few silk sutures are inserted to assure its closure, beginning medially and attaching the lower border of the ligament to the periosteum of the pubic bone and the pectineus fascia and muscle, care being taken not to injure the femoral vessels in their sheath. The cut margins of the external oblique are sutured to the underlying iliacus and internal oblique muscles. The abdominal wall is not weakened by this cutting of the external oblique.

The Surgical Treatment of Gunshot Wounds of the Chest.—Davies (*Lancet*, January 29, 1916, p. 232) writes concerning his experiences at the Third London General Hospital and the University College Hospital, his colleagues at the latter hospital allowing him to see and to treat all the cases suffering from wounds of the chest admitted to the military wards. The number of cases of hemothorax was very large and the previous experience so small that this lesion was of great interest. It is rarely possible to recognize the source of bleeding when it is in the chest or lung. The blood in the pleural cavity may be mainly fluid or a massive clot; it may be complicated by the presence of gas or a serous effusion or by infection. Extensive clotting occurs chiefly in shell or shrapnel wounds, from the extensive laceration exposing the blood freely to the action of the tissue ferment and to fragments of rib, or the introduction of portions of clothing. The blood of a hemothorax when caused by a penetrating bullet wound is mostly fluid. In the majority of these cases there is a deposit of fibrin, the amount varying in different patients. Early and, if necessary, repeated exploratory puncture is essential to the successful treatment of these cases. Without it it is not possible to differentiate in the majority of cases between a simple pleural effusion, a hemorrhagic effusion, a fluid hemothorax, a clotted hemothorax, or at times an infected hemothorax. A small quantity of fluid blood may be rapidly absorbed. Larger quantities, a pint or more, must take longer, the rate of absorption varying greatly. Davies advocates the complete removal of the fluid blood by his "oxygen replacement" method. The intrapleural pressure recorded continuously by a manometer is under absolute control. The oxygen replaces the fluid as it is withdrawn and prevents the development of a high negative pressure, which is the cause of all the

danger and distress. Clotted but uninfected blood, requires an opening in the chest wall with the removal of about 5 cm. of rib. If there is no evidence to suggest infection the wound is closed in layers to prevent leakage of air. The air admitted during the operation is replaced by oxygen as above. An infected hemothorax must be drained freely by removing a portion of a rib. The removal of foreign bodies from the lung should not be undertaken unless they are producing definite symptoms which are likely to be progressive, and even than the operation should not be done until the initial reactionary inflammation has subsided.

THERAPEUTICS

UNDER THE CHARGE OF

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The Intraspinal Treatment of Syphilis of the Central Nervous System According to the Method of Swift and Ellis.—DEXTER and CUMMER (*Arch. Int. Med.*, 1916, xvii, 82) have given 59 intraspinal injections of autosalvarsanized serum in 10 cases. Following these injections, they have seen no symptoms, temporary or permanent, which could in any way be attributed to injury to the central nervous system. There have been no deaths, paralysis, or bladder disturbances. Two of the patients have experienced no discomfort from the procedure. When gastric crises or lancinating pains exist, attacks of pain, in all ways similar to the preëxisting crisis are apt to follow the injections. These crises usually follow the treatment after an interval of from two to four hours and they are often very severe. Their duration is usually short, and they are followed by much increased periods of freedom from pain. As the treatment continues these postoperative attacks become less and the spontaneous crises often disappear entirely. It is of interest to note that those patients who have had these reactions of pain following the treatment have shown greater and more rapid improvement than those who had no discomfort from the procedure. The authors found that the increased globulin content in the spinal fluid is very resistant to treatment. The pleocytosis disappears rapidly. Their experience has been that the Wassermann reaction in the spinal fluid is the most difficult of the laboratory findings to influence. The reaction often persists in the larger doses of spinal fluid, long after the other laboratory findings have come within the normal limits. The changes in the physical findings have been a partial or complete disappearance of disturbances of sensation, lessening or disappearance of ataxia and a marked increase in weight and strength. In no case have absent deep reflexes returned, and no change in papillary reactions have been observed. The abatement or disappearance of symptoms has been most striking. In every

instance in which lancinating pains were present, they have either disappeared completely or have diminished so much that they have ceased to be a real annoyance. Gastric crises and vesical incontinence have also been favorably influenced. The results in 6 of these 10 cases have been a symptomatic improvement so emphatic that the patient's economic efficiency has been restored. They are able to work and to enjoy life to all intents and purposes as normal individuals. They feel that the best results will be obtained in cerebrospinal lues, and in tabes of the early or moderately advanced types. In far advanced tabes the results are in most cases dubious to say the least. Their own experience with paresis is too limited to make any generalization. It seems probable to them, however, that very little can be done to improve permanently a paresis once it is well established. In concluding, Dexter and Cummer feel that they can state fairly that the Swift-Ellis method is safe when the original technic is followed out to the letter. The claim of the originators that it is a valuable adjunct to the treatment of syphilitic involvement of the central nervous system is sustained as far as tabes dorsalis and cerebrospinal syphilis are concerned. It is a method which is not essential in all cases, but which applied carefully and controlled intelligently will bring about definite amelioration in symptoms and in laboratory signs where other accepted modes of attack have failed.

Mercury Elimination in Bichloride Poisoning.—Vogel and Lee (*Med. Record*, 1916, lxxxiv, 58) have found that the elimination of mercury in cases of acute bichloride poisoning may continue for periods of time ranging from a week to several months, and treatment should be continued until it has been shown that elimination of the drug is ceasing. The excretion usually continues longest from the bowel and systematic flushing of the large intestine should always be carried out, but the gastric mucosa and the skin are also important as channels of elimination and should be utilized in order to spare the renal epithelium.

The Nature of Liquid Petrolatum.—Brooks (*Jour. Am. Med. Assn.*, 1916, lxvi, 24) says that although the crude petroleum obtained from the world's various producing districts vary greatly in composition, the refined oils intended for internal administration are essentially of the same compensation. Hence there can be no different therapeutic effect obtained from the Russian variety than from the American. He notes that the internal use of the lighter oils, lighter than the specific gravity of 0.885 is to be condemned owing to the fact that annoying leakage is much more common with the lighter oils. Leakage will rarely result if only the more viscous oils of 0.885 specific gravity or heavier, be employed for internal use. The important tests in order to determine the suitability of various preparations of liquid petrolatum are undoubtedly taste, keeping quality, and viscosity. The specific gravity is roughly a measure of the viscosity and it may be substituted for the viscosity determination. One of the most important tests to make is for keeping quality. Many oils are perfectly colorless and tasteless when freshly prepared, but after standing, particularly if exposed to the light, acquire an objectionable taste and a light green color. Exposure to daylight in loosely stoppered bottles

will develop very marked differences in oils which originally are excellent in quality, within from four to ten days. The author has found that masticating the oil with ordinary white bread will bring out any petroleum taste that may be present. This test is very delicate and makes it possible to eliminate oils with this objectionable taste. Brooks does not believe that various chemical tests that have been proposed to test the purity of liquid petrolatum are of any value whatever. He believes that the simple tests he has suggested are easily sufficient to determine the relative merits of different oils. The freezing test for detecting the presence of paraffin has also been proposed; but if paraffin does not separate from the oil at room temperature, it certainly could not do so in the body. The presence of a small amount of paraffin indicates that the oil has probably been prepared from one of the so-called "paraffin base" crudes, and does not indicate an adulteration.

Sodium-salvarsan.—WECHSELMANN and DREYFUS (*Münch. med. Wchnschr.*, 1915, lxii, 177, 178) report their clinical tests of a new salvarsan preparation given them by Ehrlich for trial. This preparation is called sodium-salvarsan and chemically is practically the same in fixed form as is obtained by adding alkali in the preparation of solution of salvarsan for intravenous injection. Their experience with this new preparation extends over a period of one and a half years. They both recommend it very highly on the ground that it has the same clinical action as the original salvarsan while it is readily soluble and therefore lends itself easily to intravenous injections. Sodium-salvarsan contains about 20 per cent. of arsenic and is a yellow powder which darkens on exposure to air and becomes insoluble and very toxic, hence it must be used in fresh solution as is the case with neosalvarsan. Solutions of sodium-salvarsan are alkaline and for that reason they are not to be recommended for intramuscular use. Both authors recommend the giving of sodium-salvarsan in doses of from 0.3 to 0.6 gram, two or three times a week. They have given in certain cases as high as forty and even fifty doses, but as a rule, from 4 to 7 grams are sufficient. They say that sodium-salvarsan injections give rise to fewer reactions than either of the other two forms of salvarsan. Wechselmann says he uses it freely in a great many conditions in which previously it was considered risky to try salvarsan therapy. He mentions among such complications chronic nephritis, optic neuritis, etc., and says that in certain cases he has noticed that albuminuria has improved following the use of sodium-salvarsan. Wechselmann considers that it is very important to use pure salvarsan therapy as he believes that the combined treatment has a tendency to increase the toxicity of the salvarsan to the danger point. He also does not approve of giving sodium salvarsan in concentrated solution by a syringe but prefers to give it in a solution, using 10 c.c. of a 0.4 per cent. salt solution for every 0.1 gram of the drug. Dreyfus, on the other hand, prefers to give it in concentrated solution in distilled water by means of a glass syringe, the total amount of fluid being about 30 c.c. He also strongly favors the combined treatment, using two doses of sodium-salvarsan and one of mercury per week. They both claim that sodium-salvarsan combines the more intensive action of salvarsan on syphilis with the simple technic of neosalvarsan.

An Experimental Study of Lavage in Acute Carbolic Acid Poisoning.—MACHT (*Johns Hopkins Hosp. Bull.*, 1915, xxvi, 98), on the ground of experimental work on animals, says that the efficiency of lavage in phenol poisoning depends on the quantity of poison taken, on the time after poisoning that the lavage is begun, and in the solution used for washing the stomach. A strong solution of sodium sulphate appears to be the most useful for the purpose; next in efficiency comes plain water. The influence of alcohol in phenol poisoning depends on the time of its administration. An animal that is previously intoxicated with alcohol can withstand better the effects of phenol taken afterward. On the other hand, alcohol administered to an animal after poisoning with phenol will aggravate the symptoms and hasten death. The use of alcohol in carbolic acid poisoning should therefore be strongly discouraged.

PEDIATRICS

UNDER THE CHARGE OF

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Vascular Diseases in the Young.—CHARLES W. CHAPMAN (*Brit. Jour. Child. Dis.*, 1916, xiii, 97), in reviewing this subject, shows that arteritis is not infrequent in infancy and adolescence. This condition affects normal development and tends seriously to shorten life. From a large number of reported cases it would appear that inherited syphilis is probably the basic factor in the majority of cases although the condition is also caused by infectious diseases such as rheumatic fever, diphtheria, scarlet fever, pneumonia, and tuberculosis. Among the reported syphilitic cases are aneurysm of the abdominal aorta in a fetus of eight months and seven cases of thoracic aortic aneurysm under ten years, many of them associated with arteritis. Thickened and tortuous arteries, often with ventricular hypertrophy and accentuated second aortic sound were found in toxemias, such as intestinal or nephritic in children under the age of puberty. Under proper treatment most of these signs disappeared. Numerous cases of calcification of the aorta and peripheral arteries are recorded in infants as young as six months and in children. Not all of these were due to syphilis. After a detailed account of four cases of arteritis in infants and young children, three of which were due to syphilis, the author discusses the diagnosis, prognosis and treatment. Under the first, arterial thickening should be looked for in the brachial and femoral arteries besides in the radials. Arteritis causes swelling and pain in the affected limb and aortitis shows a diminished resonance over the manubrium. History of syphilitic infection, stigmata or a positive Wassermann reaction are important factors. Arteritis due to toxemia from overfeeding or from the intestines usually improves under mercurial purges. The treatment is that of the infection causing the arteritis. Fixation and moist heat

for involved limbs, mercurial purges and correcting dietetic errors in intestinal toxemia and appropriate treatment in syphilitic cases are called for.

The Prevention of Respiratory Disease in Early Life. — ROYAL STORRS HAYNES (*Arch. Pediat.*, 1916, xxxiii, 81) emphasizes the fact that respiratory diseases in early life have not been diminished as have intestinal diseases. The infectious cold is most vicious probably in its sequelæ and complications and in its attendant lowered vitality which encourages other diseased conditions. The first five years of life are particularly susceptible partly on account of the effects of rickets, measles, pertussis and adenoid growths. Also the narrowness of the respiratory passages plays an anatomical part. Lowering of resistance is the primary cause and is brought on usually by exposure to cold, fatigue, auto-intoxication, poisoning by food or chemicals. Among the factors to be overcome is the dust nuisance. Oiling and watering of streets tends to prevent outdoor dust. Vacuum cleaners, dustless dusters, wet-sweeping and the use of rugs instead of carpets is desirable. The smoke of large cities is an irritant and should be minimized as it markedly increases respiratory diseases. Crowding in houses, street cars, trains, theatres, etc., is a great factor and its elimination tends to control a large part of respiratory diseases. The regulation and control of measles and pertussis, especially the early recognition and isolation of cases, the isolation of susceptible contacts and increased control in the resporting of cases would cut down the respiratory conditions attending these diseases. Regulation of attendance at school of children with respiratory affections is important. There is no such thing as a "little cold." "Open air" schools and "open window" schools minimize respiratory conditions. Proper care of children in the home through hygiene and sanitary measures, to keep up the resistance of the child is the most important prophylactic measure. Personal hygiene and the factors of food, clothing, ventilation, sleep and bathing are all important. The proper hygiene of the mouth is important as bacteria grow well there. The destruction or exclusion of the infecting organism and the preservation of resistance of the individual especially are the most important factors.

Mitral Stenosis in Young Children.—MURRAY H. BASS (*Arch. Pediat.*, 1916, xxxiii, 107) describes two cases of mitral stenosis in children, one in a boy of ten years, with no etiologic factor except a normal case of measles, recognition of the condition at the sixth year, no symptoms referable to the heart and a negative Wassermann and von Pirquet. However there is marked stunting of growth and a mentality below normal. The other case, of a boy, seven and one-half years old, had cervical adenitis, has had scarlet fever mildly, showed a positive Wassermann, and was markedly under-developed and puny. The only signs of a cardiac condition were occasional attacks of cough and dyspnea. Antisyphilitic treatment caused an improvement in his general condition and appetite and his cervical adenitis, his weight and stature practically remaining the same during almost two years following. The lack of development shown in both these cases is due presumably to the cardiac disease. In mitral stenosis in children

where no signs of insufficiency are present, syphilis should be thought of and a Wassermann done. Cardiac disease, especially valvular stenosis exerts a considerable influence on growth. From the literature on this subject one concludes that mitral stenosis has been observed at autopsy in infants; that it has been observed in children over five years old with no apparent etiological factor present though without sufficient evidence of their being "congenital"; no case of mitral stenosis has been found reported in children between the ages of infancy and five years. Weber suggests that in the small size of the body in these cases one sees a "conservative adaptation or conservative hypoplasia of the whole body—natures attempt to limit the growth of the patient in accordance with the limited blood supply."

Treatment of Scarlet Fever with Fresh Blood from Convalescent Patients.—ABRAHAM ZINGHER (*New York State Jour. Med.*, 1916, xvi, 112) reports the results of injecting fresh blood from convalescents into the muscles of scarlet fever patients. This method for the intramuscular injection of whole blood represents a convenient way of giving a patient human serum. The following muscles are chosen and a syringeful (one ounce) of blood is injected into each place: the gluteal regions, the outer regions of the thighs, the calves and the triceps muscles. The blood is taken from the median cephalic vein of the donor. From four to eight ounces of blood are taken. Absorption from the muscles takes place rapidly and usually without further local irritation. Fourteen cases of toxic scarlet fever were injected. They were selected out of 650 admissions on account of the severity of symptoms. Of the 14 cases 4 died, being almost moribund on admission. The amount of blood injected varied from 75 c.c. to 250 c.c. Larger quantities, from 8 to 10 ounces have been found to exert a distinctly beneficial effect in some very septic late cases. The effect of the blood in the 10 recovered cases was as follows: Some of the cases showed a very definite relationship between the injection and a critical drop in temperature with improvement of the circulation, general condition and especially mental condition. The reaction begins from two to four hours after injection and is completed in nine to fourteen hours. It has no effect on secondary septic conditions. The pulse becomes stronger, steadier, and slower. Cardiac symptoms and the cyanosis improve and respiration becomes more normal. General condition improves perceptably and subjective symptoms disappear. Rash fades rapidly. If any benefit is to be derived from convalescent blood its action must be brought into play early, before toxemia is overwhelming. Addresses of convalecents can be kept on record and donors in this way may be sent to private homes. Considerably more therapeutic work of this kind must be done before definite conclusions as to the value of this treatment can be made.

OBSTETRICS

UNDER THE CHARGE OF

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The Aseptic Care of the Umbilicus in the Newborn.—MÜLLER (*Ztschr. f. Geburts. u. Gynäk.*, 1914, lxxvii, 3) reports the results of methods employed in the hospital at Basel, Switzerland, in the service of von Herff. The material included 4000 newborn children. He concludes that it is impossible to escape a typical surgical aseptic process in the healing of the umbilical wound. He believes that this region becomes infected in the child's passage through the vagina and that one can distinguish the line of demarcation between necrotic tissue and connective-tissue which is undergoing mummification. All that one can do then in the interest of the child is to protect it against the most pathogenic and virulent bacteria. For this purpose, the ordinary daily bath is omitted. The umbilicus after its first dressing remains undisturbed for ten days, unless a foul odor, excessive secretion or fever develop. The child's body may be sponged and cleanliness maintained without disturbing the umbilicus. The results of this method are the rapid granulation of the umbilicus with a minimum of cases of infection. The stump of umbilical cord affords especially desirable material for the growth of bacteria. The tissue is rich in water and gelatinous in composition. To avoid trouble, the cord should be cut as short as possible, the stump crushed and so dressed as that air can gain access freely during the process of healing. The granulation tissue at the umbilicus is exceedingly sensitive to chemical and mechanical irritation. All forms of dressing or applications should be so applied as to make the least possible irritation. The method used in the Basel Clinic is as follows: As soon as pulsation ceases in the umbilical cord, which should inevitably be waited for except in cases of operation, or where immediate necessity is present, the cord is ligated 8 cm. from the umbilicus with linen tape 0.5 cm. broad with double ligature and then is severed. The cord must not be touched by the midwife of physician except with hands thoroughly disinfected with alcohol or with sterile material. As soon as the child is taken to the nursery for its initial bath von Herff's clamp is applied. This instrument is shaped like a hemostat with jaws considerably longer, serated and bent at an angle. The instrument weighs 12 gms. It is applied very slowly upon the stump of cord so that the vessels are not torn and thus hemorrhage afterward is prevented. The clamp is applied close to the skin. The vernix is removed with sterile olive oil, the clamp removed and the cord tied close to the skin at a point where the cord has been thoroughly compressed by a ligature. The child is then bathed and the cord cut close to the ligature. The umbilicus is dressed with a sterile round compress of muslin kept in position by an inherent ring. This dressing remains undisturbed for ten days. In experimenting various substances were tried and the effect noted. Thus: balsam of Peru,

thymol in alcohol, thymol in vaseline, noviform, sugar and hydrogen peroxide were all tried. Of all the materials employed, balsam of Peru gave the best result; sugar next; 10 per cent. noviform salve without cotton next; and hydrogen peroxide last. Among the material observed, were four cases of umbilical infection. All of them were mild in character and speedily disappeared under applications of alcohol. In reviewing the results of the clinic showed that in the last 5000 children treated from 1912 to 1914, there was no case of umbilical infection. In prior years, the mortality from this condition was estimated at 0.07 per cent. in 10,000 children.

Rupture of the Uterus During Pregnancy.—MEYER (*Arch. mens. d'obstet.*, August, 1915) reports three cases of rupture of the uterus during pregnancy. The first was in a woman, aged thirty-five years, who had had nine pregnancies previously, three terminating prematurely. About six weeks before term, the patient was suddenly seized with prostration, abdominal pain, the discharge of a little fluid from the vagina and the development of shock. When brought to hospital, the patient was without appreciable pulse, the abdominal condition could not be clearly made out by palpation but the abdomen was immediately opened. There was a large quantity of blood in the peritoneal cavity, the fetus was in Douglass's pouch. The body of the uterus had ruptured from above downward near its left border and at the point of rupture had become inverted. Hysterectomy was practised but the patient succumbed. An examination of the uterus could assign no cause for the accident. The second patient was a multipara who came into labor with inefficient uterine contractions. The abdomen was greatly enlarged, exceedingly painful on palpation. A physician who was summoned administered morphin and chloral but the hemorrhage continuing, the patient was brought to hospital as a case of placenta previa. On admission, her clothing was soaked with blood and Momeberg's bandage was immediately applied, arresting the hemorrhage. While the patient was being prepared for abdominal section, she died. Autopsy showed a longitudinal rupture in the body of the uterus near the right border. Examination of the uterus failed to reveal any histological changes in its substance. His third case (also a multipara) who had had no labor pains but who, upon going to a toilet, was suddenly taken with severe abdominal pain. The patient was pale with a very feeble, regular pulse, the abdomen very painful upon palpation. The urine contained albumin and casts, there was no hemorrhage nor uterine contraction. Morphin was given to relieve pain, but the symptoms continued and the patient gradually grew worse. On opening the abdomen, there had been considerable hemorrhage with rupture at the fundus. The child was living but died shortly after birth. The mother made a tedious but complete recovery.

The Causes Which Stimulate the Mammary Secretion During the Puerperal Period.—ZULOAGA (*Arch. mens. d'obstet.*, September, 1915) has studied the factors which stimulate the secretion of milk. He describes the case of a patient pregnant about four months threatened with abortion in whom he used a tampon of gauze. The patient had strong uterine contractions and on removing the packing a cotyledon of the placenta

was adherent to the gauze. Two days following the condition of the patient was satisfactory but on the third day there was a rise of temperature and pulse with considerable secretion of milk. The breasts were so swollen that the movement of the arms was painful. The secretion of milk lasted nearly three weeks after the abortion. The patient stated that she had been delivered of a child five months before and that the midwife in attendance had delivered the placenta with the hand and that there had been no possibility of conception since that time. Evidently this retained portion of placenta which had been removed with the gauze was the cause for the free secretion of milk.

The writer also reports the case of a multipara pregnant for about six months, who expelled a fetus of about three months, mummified, with a placenta corresponding in size and development to five months. The placenta showed a subchoreal hematoma. The patient made a good recovery but two days after the expulsion of the dead fetus, the secretion of milk developed in abundance and proceeded for sometime. His third case was that of a multipara who believed herself pregnant seven months when the active movements of the fetus ceased. Two days later there was a secretion of milk, which persisted for six days. A seven months macerated fetus was expelled accompanied by the placenta and this showed areas of coagulation necrosis. These cases seem to indicate that the substances formed in the placenta and transmitted to the circulation furnishes a stimulus which excites mammary secretion. The writer states that the crisogonous hormone which stimulates the secretion of milk is secreted by the myometral glands. It is not thought that the fetus has any influence in determining mammary secretion. During pregnancy the internal secretion of the myometral glands goes to the placenta, thence to the fetus, determining certain crises of development in the newborn to which Bar has called our attention. When the direct connection between the placenta and the uterus is interrupted the secretion of the myometral glands passes into the blood of the mother and stimulates mammary secretion. Uterine involution is favored by the passage of the crisogonous hormone into the maternal blood. These substances are found in greater or smaller quantity in the fetus, placenta and uterine tissue and this fact explains the results obtained by those who have used these substances in stimulating mammary secretion.

GYNECOLOGY

UNDER THE CHARGE OF

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Radiotherapeusis in American Gynecology.—The application of radiotherapy to various gynecologic conditions had become a well established practice in Europe before the outbreak of the war, the

leaders in this movement being several of the large university clinics of Germany. Taken up to a considerable, but somewhat less degree in France, radiotherapy was for some years looked at with much scepticism by the gynecologists at large in this country, and it is only comparatively recently that reports in any number have appeared in our literature concerning the gynecologic uses of the Roentgen-ray radium, and similar agents. The pioneer in this work in this country was Kelly, of Johns Hopkins; he is able to furnish statistics that both quantitatively and qualitatively compare favorably with those of any of the foreign clinics. In a recent resumé of some of his experiences with radium as a therapeutic agent in various malignant conditions, KELLY (*Am. Jour. Surg.*, 1916, xxx, 76) says that from January 1, 1909 to January 1, 1915 he has treated 213 cases of carcinoma of the cervix uteri. Of these, 10 were operated upon; 4 more might have been considered operable, but for various reasons were not operated upon; the remaining 199 were inoperable, either primarily, or were inoperable recurrences after operation. The 10 operated cases were subsequently subjected to prophylactic radiation, and all are apparently well at intervals ranging from six months to two years since operation. Of the remaining 203 cases, 57 are "clinically cured," 109 markedly improved and 37 not improved. In judging these results, it must be taken into consideration, however, that only 1 case of the entire series has passed the five-year limit, now pretty universally agreed upon as the minimum time in which we may speak of a "cure;" the others range from six months to four years since treatment. Kelly says that as a result of his experience in these cases, the following rules have been evolved as being the expression of his present policy: (1) Operate on every operable case, estimated as a good risk, as heretofore; (2) radiate for four to six weeks after operation; (3) do not operate on borderline cases, but use radium first, for the disease practically always returns after operation in these cases, while many are curable by radium; (4) radiate all advanced inoperable cases; for many of these too are curable, or can be shrunken down so as to become good risks; (5) where there are metastases up into the abdomen radiation may give great relief and a temporary return to apparent good health, but it will not cure. Kelly points out that it is very important to keep all these cases under occasional observation for some years, as a slight relapse is not infrequent, and as a rule responds readily to another application of radium. He feels that even if radium never actually cured a single case, it would nevertheless be an inestimable boon because of the prolonged relief which it gives from pain, with checking of offensive discharges, and general improvement in health and interest in life that it affords to sufferers from uterine cancer. Impressions obtained from a much smaller series of cases, observed over a shorter period of time, have been reported by MILLER (*Surg., Gynec. and Obst.*, 1916, xxii, 437) at a recent symposium of the Chicago Gynecological Society on Cancer of the Uterus. Since May, 1914, Miller has treated 26 cases of inoperable and recurrent cancer of the cervix with radium, and has followed the cases up to December, 1915. It is obvious, therefore, that absolutely nothing can be said as to ultimate results. Of 15 inoperable cases treated solely with radium, 4 have died and 2 are slowly succumbing; 5 are at present apparently free subjectively and

objectively of the disease; 4 showed evidence of returning trouble about six months after treatment, but have responded so far to further applications. In common with others, Miller has been astonished at the tremendous local benefits observed in practically all cases in the way of checking hemorrhage and discharge, and deodorization. In a number of cases excochleation and cauterization had been practiced a few months prior to the institution of radium treatment, but Miller does not approve of this procedure, since he is convinced that in these cases a longer time was required to check the local symptoms, and the subsequent histories do not show that they remained well any longer for having had the preliminary cauterization. In 6 cases radium was applied to malignant areas reappearing in the vaginal vault after hysterectomy —an extremely hopeless condition under ordinary circumstances. In four of these patients the growth promptly responded to the treatment, but as yet nothing can be said as to the ultimate outcome. In one case the mass soon disappeared, but the patient soon died from an infected kidney, and in the sixth, local masses have responded twice within the past year, but the patient is gradually going down hill. Miller emphasizes that his paper can be considered merely a preliminary report of experiences to date, but considers that while they in no way prove that radium can cure cancer, the results so far are superior to any other method that he has used in similar cases. His technic is to employ from 75 to 85 milligrams of radium element, endeavoring to give 3000 to 5000 milligram hours within a week or ten days, further applications being made a month later according to the indications. The question of gynecologic radiotherapy by means of the Roentgen-ray tube rather than radium has recently been discussed by LANGE (*Am. Jour. Roentgenol.*, 1916, iii, 72), who reports the results obtained in a series of 50 cases of benign conditions, such as menorrhagia, dysmenorrhea, and uterine myomata. He says that since the perfection of the Coolidge tube this form of treatment has been put on a much more satisfactory basis than formerly, since many of the technical difficulties of applying sufficient dosages have been removed. Whereas with the old equipment most roentgenologists who had interested themselves in gynecologic work had concluded that forty years was about the lowest age at which the artificial menopause could be produced with certainty, with the Coolidge tube there is no age limit beneath which it is not feasible to produce this result at will. In his series there were two patients of seventeen, and one of nineteen years, in whom an apparently permanent menopause was produced without difficulty. He therefore feels justified now in promising definitely that this result can be achieved in all cases in which malignancy, or inflammatory conditions such as pus tubes, can be excluded. In his series of 50 consecutive cases cessation of menstruation was secured in all in which it was desired, irrespective of age, and this as a rule exceedingly promptly. Lange says he has found it to be a safe working rule that when one period is missed all treatments may be stopped, since it is almost certain that though there may be an occasional showing subsequently, permanent cessation of menstruation will finally result. The dosage required to accomplish this varied in his cases from 100 X (one treatment) to 800 X (eight treatments). In 1 case a severe menorrhagia was reduced to a condition of normal menstruation, treatment

being stopped before complete amenorrhea was reached, and the author feels that with increasing mastery of the technic this ideal result may be looked for with much greater frequency in the future.

Reno-renal Reflex Pain.—The fact that unilateral renal pain, due apparently to a definite lesion in one kidney, but referred to the kidney region of the opposite side, may occasionally occur has long been known to the profession, but owing to the rarity of the phenomenon its possibility is often overlooked, thus leading to serious errors in diagnosis and treatment. An unusually striking and interesting example of this condition has recently been studied by FOWLER (*Surg., Gynec. and Obst.*, 1916, xxii, 454) and reported before the American Association of Genito-urinary surgeons. The patient was a young woman, aged twenty-nine years, who when first seen was suffering with what appeared to be a typical attack of renal colic, the pain being confined entirely to the right side. Ten years previously she had had an attack of hematuria, followed in a day or two by a very severe attack of kidney colic, the pain being localized in the right side. Five years later, after an interval of perfect health, she had a second similar attack, since which there had been no further pain up to the onset of the attack for which she came under Fowler's care. There had never been any pain on the left side, and no vesical irritation. Examination showed no tenderness, muscular rigidity, or pain to palpation of the left kidney region, but distinct pain, tenderness, and slight muscular rigidity on the right side. A Roentgen-ray examination showed a distinct shadow opposite the cartilage between the third and fourth lumbar vertebræ on the left side; the right kidney and ureter and left kidney were negative. A wax tipped catheter introduced into the left ureter met an obstruction at a point 24 cm. from the ureteral orifice, but by rotating could be passed by it into the kidney pelvis. Examination of the catheter on removal showed deep spiral grooves cut in the wax, evidently due to a stone in the ureter at a point 24 cm. from the bladder orifice, and just corresponding to that indicated by the Roentgen-ray. Catheterized specimens from each side showed a heavy ring of albumen and many leukocytes on the left, with no albumen and no leukocytes on the right. The output of urea was also greatly diminished on the left. In view of these findings, Fowler considered the diagnosis of stone in the left ureter justified, in spite of the fact that all symptoms had been on the right side. This diagnosis was confirmed at operation, an oblong, grayish-white stone having a surface bristling with sharp pointed crystals being removed from the left ureter. Convalescence was satisfactory, and there has been no recurrence of the pain in the right side up to the time of writing, eleven months after operation. The case above outlined is certainly of great interest, not so much from the standpoint of its curiosity, but from the emphasis that it throws upon the necessity of the most thorough examination by all the modern diagnostic means at our disposal of both kidneys and ureters in all cases of suspected renal or ureteral lesion. Had attention in this case been directed merely to the apparently affected side, the condition would not have been cleared up, and a serious but entirely useless operation might have been performed upon an entirely healthy kidney.

OTOLOGY

UNDER THE CHARGE OF

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Acoustic Injury and Personal Prevention of Occupational Deafness.—Numerous writers, including SIEBENMANN (*Korrespond. f. Schweiz. Aerzt.*, 1915, No. 13), have given evidence, on the basis of experimental observation, that acoustic violence results in pathological changes in the labyrinth, the injury being primarily exhibited in the organ of Corti, later the efferent nerves and the proximate ganglia and finally in the body of the cochlear branch of the auditory nerve. The degenerative process in the nerves is to be regarded as secondary and progressive, and in reference to location, varies with the character and the path of intrusion of the acoustic shock. In reference to the question as to the direction of access of the sound waves to the labyrinth and the possibility of communication of acoustic shock through the medium of the body or the major access through the oval window, the author made elucidative investigations. By extraction of the incus, the sound transmission through the middle-ear mechanism was done away with, and in the animals thus treated, exposure to loud noise produced no intralabyrinthine injury, the conclusion being that aerial sound conduction through the sound-transmitting apparatus of the middle ear was the major path of transmission and that, for personal protection from occipital noise, the stoppage of the external auditory canal is of primary importance, the isolation of the body of the workman, by means of felt soles and rubber gloves, being unnecessary.

Aural Implication in Diabetes Mellitus with Especial Reference to the Internal Ear.—In all of the cases in which protracted observation was possible there was evidence of a slowly progressive depreciation in the hearing power, the result of the cumulative degenerative change in the cochlear nerve and the cell elements of the organ of Corti. The symptoms of most prominence, according to the observations of EDGAR (*Monatschr. f. Ohrenh.*, 1915, xlix), in addition to the impairment of hearing, were the occurrence of subjective sounds and attacks of vertigo; in the great majority of the cases both ears were similarly affected, so far as impairment of hearing was concerned. In but 1 out of the 52 cases recorded was the impairment of hearing of sudden onset, in all the others the beginning of the impairment and its progress had been unappreciated, indeed the majority of the patients made no unsolicited reference to the hearing which was found to be impaired only upon examination and test. This observation may, in the opinion of the author, be in part accounted for by the recognized fact that, in long-standing cases of diabetes, there is a general weakening of the reflex functions including a certain acoustic dulness so that a creeping progressive deterioration of the hearing power would not be appreciated. In very nearly one-half of the cases subjective sounds

were reported in one or in both ears, more frequently intermittent, but in some cases continuous In 3 cases, for six months under observation, the subjective sounds at first reported ultmately disappeared. In 6 of the cases there was labyrinthine vertigo. In 3 of these the attacks were of short duration only and apparently the sequence of some psychic excitation or muscular exertion. In 1 case only were the attacks fulminant. Spontaneous nystagmus was demonstrated in only 1 or 2 cases and then in moderate degree. In about one-quarter of the cases there were disturbances of equilibration in a very moderate degree and there were only 3 cases in which the patients could not maintain the Romberg position or balance upon one foot. The diagnosis of the aural implication in diabetes presents no difficulties. The history in any given case, together with the results of the acoustic tests, a positive Rinné, lessened hearing by bone conduction, a nearly normal hearing for tones of medium low pitch, lessened hearing for tones of high pitch, aerially conveyed, without corresponding objectively observable cause in the middle-ear sound-transmitting apparatus, coupled with a general physical examination, eliminative of other general causes for the labyrinth affection, are distinctly determinative of the true condition. As concerns the course and the prognosis of this peripheral concomitant of diabetes, it is especially chronic in its development and continuity; the patients are rarely able to indicate, even approximately, the time of the beginning of the aural symptoms; a moderate degree of impairment of hearing passing unnoted and its gradual progress, without acute variations, presenting nothing especially worthy of remark. In 1 case of a high grade of deafness, ten weeks' observation showed no change. In 3 cases of moderate impairment of hearing and 1 case of a medium grade of impairment, an examination, when repeated at the end of two months, showed a slight gain in the general hearing power, which gain was subsequently lost, the improvement being coincident with persistence in a strict antidiabetic diet and the urine being free from sugar. In reference to treatment it was uniformly observable that there was an improvement in the hearing so soon as the urine was free, or nearly free, from sugar and that depreciation in hearing was found to be coincident with any subsequent increase in the sugar percentage in the renal excretion. Local aural treatment is of no avail in these cases. Galvanization of the acoustic nerve has been suggested and applied without, however, any demonstrably good effect; the labyrinth affection in diabetes being intimately dependent for its course and progress upon the causative disorder. The fact that the impairment of hearing in cases of diabetes is so moderately in evidence in its beginning and the very positive dependence of the intralabyrinthine evidences upon the causative renal condition make the observations of the author and his following conclusions of especial value to the general practitioner since, in the paucity of aural manifestations there would be a comparatively lessened liability of reference to special investigation. The frequency of disease of the internal ear in diabetes and the fact, established in many cases, of an improvement in the hearing coincidently with the entire or comparative freedom of the urine from sugar and, contrariwise, a depreciation in hearing together with an increase in sugar percentage in the urine may be taken as indubitable evidence of the etiological relationship of the two phenomena. In a por-

tion of the cases there was a degenerative change in the internal ear implicating the auditory nerve the result of a toxic neurolabyrinthitis, while in still other cases the pathological changes in the labyrinth were the consequence of the arteriosclerotic changes in the bloodvessels, to which diabetics are especially prone.

Experimental Investigations into the Traumatic Pressure Effect of Explosions.—Recent experience in military operations shows that serious injury may be effected by windage or air compression incident to the immediate vicinity of shells in flight, even to the extent of fracture of the vertebræ in a man sitting in a bowed position, of which the scalping or denudation effect is a further example. F. Rusca (*Deutsch. Ztschr. f. Chir.*, cxxxii, p. 315) endeavored to explain these effects in parallel by studying the influence exerted by gas and water compression upon rabbits and fishes, it being found that the influence exerted, through these media, in addition to the frequently recognizable rupture of the drum-head, resulted in serious injuries to the skull and to the brain, and to the latter when the cranium remained intact, as exhibited frequently during the present war in the form of hemorrhages at the base and at the convesity of the brain. The variety of injuries produced, including the ruptures of, and ecchymoses in, the membranous labyrinth is explained by the author by the radiated as well as by the direct pressure effect.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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The Prevalence of Trachoma in Kentucky.—In 1912 a survey made by the U. S. Public Health Service of seven counties in the mountain region of Kentucky, showed that 12.5 per cent. of the population of the counties examined were suffering from trachoma. This survey has been continued and the results of the later work have been published (*Public Health Reports*, March 5, 1915). It was found in the survey of twenty-three counties, 18,016 persons being examined, that 1280 cases or over 7 per cent. of those examined were suffering from trachoma. In some counties the percentage of persons found infected was as high as 26.4 per cent. while in others it fell to about 3 per cent. The majority of those examined were school children and the findings may be taken as representing fairly accurate conditions among adults. Almost all those examined were whites, as the negro population is very small in

the mountain section of Kentucky. Inasmuch as the bulk of the population in these counties comes from old American stock, foreign immigration cannot be blamed for the prevalence of the disease. The U. S. Public Health Service regards its estimate of 33,000 cases in thirty-five mountain counties as conservative, though approximate, and has established hospitals at various points for the treatment of the disease and the education of the general public as to the means of its prevention. Trachoma undoubtedly exists in many other places in this country. It is certainly widespread among the Indian tribes and the Public Health Service is endeavoring to eradicate the disease and prevent its spread.

The Experience of the New York City Health Department with Typhoid Immunization.—HARRIS and OGAN (*Department of Health of the City of New York Reprint No.* 22, January, 1915) draw the following conclusions: (1) The accurate observations recorded in hundreds of thousands of cases leave no doubt as to the preventive powers of antityphoid vaccination in all but a relatively insignificant number; (2) In those subsequently affected it strikingly decreases severity of the disease and the mortality; (3) Severe reactions, if one makes observations from extensive studies (the only correct way) are rare; (4) To avoid severe reactions one must observe carefully several precautions, as follows: (*a*) Never administer it to any but the healthy; (*b*) To permit of slow absorption, avoid puncture of a vein, or intramuscular injection; (*c*) Clean syringe and sterilize the area for injection, using tincture of iodin for the latter purpose; (*d*) Children, especially, are to avoid exposure to the sun following treatment; (*e*) Avoid administering it during the menses or pregnancy; (*f*) Allow no hard work or indulgence in alcohol immediately after the injection; (*g*) Avoid reinjecting in indurated areas; (5) Severe reactions have never left permanent injury; (6) When the incubation period has begun, the time for antityphoid immunization has passed. The vaccine is a preventive of typhoid fever, and not a typhoid antitoxin; (7) Long exposure to overwhelming doses of typhoid bacilli as in those who are in close contact with cases and especially in epidemics, may nullify the immunization powers of antityphoid vaccine, and an attack may therefore incidentally follow one or more injection; (8) Chronic illness (tuberculosis, etc.), as well as debility from other causes, and fatigue and exhaustion also predispose to severe reactions; (9) Injection after intimate and long exposure hasten the onset; (10) For a period of at least two years, and possibly longer, immunization is as effective in protecting from an attack of typhoid fever as is a previous attack of the disease itself; (11) Infections may follow after a complete immunizating course of treatment, in exceptional instances in which debility and fatigue exhaust the resistant and defensive powers of the body, and when exposure to massive doses of typhoid bacilli exists.

A Survey of the Public Health Administration of the State of Washington.—The United States Public Health Service, has, in the last twelve months, been making a survey of certain State health organizations with a view of standardizing the operations of the various sanitary studies in the United States. It is hoped that the accomplish-

ment of this end will do much to bring about uniformity of action on the part of public officials and to further increase the efficiency of the various State and municipal health organizations. The results of the survey of the health administration of Washington have been published (*Public Health Reports*, February 5, 1915). The conclusion was reached that the adoption and enforcement of measures for the protection of the public health in that State have not kept pace with the economic growth of the State. An analysis is made of the various functions and activities of the Washington State Board of Health and certain recommendations are made, the adoption of which it is believed would meet the present public health requirements of that State. Briefly summarized, these recommendations are: That all public health activities now performed by the State should be brought together in a single department of health, to be subdivided into bureaus, with a commissioner of health as the administrative head and the State Board of Health as an advisory and quasilegislative body. The functions of the various bureaus are carefully outlined, and it is recommended that the State be divided into not less than fifteen health districts, each to be under a whole-time health officer of adequate training and experience in the science of public health. It is also recommended that the State be divided into three districts, each to be put under the supervision of a sanitary engineer. Provision is made for laboratories and the passage of various model laws, one for morbidity reports receiving especial attention. Up to this time the Public Health Service has made and published the results of surverys of health administration of the States of Minnesota, Maryland, West Virginia and Washington, and of the city of Baltimore. It has been announced that the service is now making health surveys of other States and of several cities.

The Milk Supply as a Causal Factor in Relation to Tuberculosis.—SHERIDAN DELÉPINE (*Journal State Medicine, Reprint*, November and December, 1914) states that it is impossible to measure accurately the amount of tuberculosis that is attributable to cows' milk because the various methods of investigation give widely different indications. There is, however, on many points, general agreement between observers; the differences relate chiefly to quantitative estimates. The information supplied by the various methods indicates: (1) That an exceedingly small number or children are tuberculous at birth; (2) That soon after birth they begin to contract the disease; (3) That the nature of the tuberculous lesions and their distribution show that before the fifteenth year the alimentary passages are important channels of infection, and that after the fifteenth year infection generally takes place through the air passages; (4) That, when the matter has been investigated, it has been found that among children suffering from tuberculosis other than pulmonary tuberculosis a great number have been fed on unsterilized cows' milk; (5) That from the lesions of children fed on unsterilized cows' milk, bacilli resembling those associated with bovine lesions are found in the great majority of cases; (6) That both the distribution of the lesions and the characters of the bacilli seem to indicate that not less than 20 to 25 per cent. of the cases of infantile tuberculosis are attributable to infection through cows' milk, and that

some results indicate a much higher proportion; (7) That experimental evidence shows that the ingestion of tuberculous cows' milk is followed by infection through the alimentary canal in the great majority of mammals on which the experiment has been made. Delèpine concludes that it appears reasonable to say that, although there is not complete agreement in the results obtained by various observers as to the exact amount of human tuberculosis attributable to the consumption of tuberculous cows' milk, there is *clear and cumulative evidence that cows' milk plays a very important part in the production of infantile tuberculosis in England and Scotland.*

The Action of Anti-pneumococci Serum.—C. G. BULL (*Proc. Soc. Exper. Biol. and Med.*, 1915, xii, 149) studied the cause of the disappearance of pneumococci from the blood, following an intravenous injection of a small amount of immune serum. He found that the immune serum actively agglutinated the pneumococci in dilutions of 1 to 500, when observed under the microscope, whereas macroscopically the agglutination titre is 1 to 80. Therefore, it was surmised that the disappearance of the bacteria from the circulating blood, following the injection of immune serum, might be due to clumping *in vivo*. Next, fragments of the organs—lungs, spleen, liver, kidney, brain, etc., were crushed and examined and clumps of pneumococci were found in all. The fate of the clumps was then investigated. By killing the rabbits at various times, after the administration of the serum, it was observed that the polymorphonuclear leukocytes englobed and digested them. The fixed cells play a small part also. Sectioned and crushed tissues gave the same results. Pneumococci from 150 c.c. of bouillon are thus destroyed within two to three hours. The smallest amount of serum that will influence the infection causes the clumping *in vivo*.

Chronic Lead Poisoning: Breeding Experiments.—C. V. WELLER (*Proc. Soc. Exper. Biol. and Med.*, 1915, xii, 157) notes that there have been frequent clinical observations of the apparent deleterious effect upon the germ plasm exerted by chronic poisoning. A majority of these cases have been found in female lead workers and in these it might be supposed that abortions, stillbirths, and early deaths of infants were due as much to the toxic effect of lead during extra-uterine development as to an actual injury to the germ plasm. In the smaller number of instances in which the male parent alone was poisoned, the resulting sterility without impotency, the stillbirths and the early deaths of offspring are difficult to explain unless they are due to blastophthoria. The work of Stockard and of Cole and Davis has shown that alcohol has a similar effect. In a recent report which appeared as the present series of experiments was being concluded Cole and Bachhuber have demonstrated that the offspring of male rabbits poisoned by lead as well as of male fowls similarly poisoned are of distinctly lower vitality than the offspring of normal males. In attempting to determine experimentally whether blastophthoria occurs in chronic lead poisoning, guinea-pigs were given repeated weighed doses of commercial white lead in capsules by mouth. These guinea-pigs were mated, lead females with normal males and lead males with normal females. In order to check the results as efficiently as possible control matings were

made of normal males with normal females under the same feeding and housing conditions as the lead poisoned pigs, and for the same reason the normal females were bred alternately to lead males and to normal males. The dosage of lead was controlled by frequent weighings in order that the general nutrition should not be seriously impaired. A total of 93 matings yielded 170 offspring. Of these, 32 matings of normal male with normal female produced 58 offspring, with an average birthweight of 81.5 gm. From 34 matings of lead male with normal female 65 young were produced with an average birthweight of 69.3 gm. Nine offspring of lead males died in the first week against 2 offspring of normal males dying in that time. Eight young of lead females were stillborn against 3 stillborn from normal females bred to normal males. From the entire series of matings the following conclusions seem to be justified: (1) In chronic lead poisoning in guinea-pigs there is a definite blastophthoric effect which can best be demonstrated upon the male germ plasm. This effect manifests itself in some instances by sterility without loss of sexual activity, by a reduction of 20 per cent. in the average birthweight, by an increased number of deaths in the first week of life and by a retardation in development such that these pigs remain permanently underweight. (2) From the apparent recovery of the germ plasm some time after stopping the administration of lead it seems that the deleterious effect must be suffered especially by that portion of the germ plasm which is undergoing maturation and not by that which is stored in the primary germinal epithelium. However, final judgment upon this point must be withheld.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Effect of Antibody Production of the Removal of Various Organs.—HEKTOEN and CURTIS (*Jour. of Infect. Dis.*, 1915, xvii, 409) carried on a rather remarkable series of experiments to determine the part played by certain organs in the production of antibodies. The experiments were performed on dogs immunized against rat blood, and the agglutinins and opsonins were determined. The control animals showed maximum antibody production on about the twelfth day followed by a gradual defervescence to the normal level on about the fortieth day.

Other animals, following an immunizing inoculation were subjected to various operations in which some abdominal or other viscus was removed. It was found that complete removal of the stomach, of the small intestine or of the thyroid did not interfere with the development of the antibodies studied. Removal of the pancreas, complicated by intussusception and rabies, showed lessened production of the immune substance. Simultaneous removal of the spleen and pancreas also inhibited antibody production simulating the removal of spleen alone. Removal of the small intestine and ligation of the mesenteric artery increased the latent period preceding the appearance of the antibodies. Adrenalectomy did not influence the antibody curve. The authors conclude that the production of antibodies is not influenced by certain disturbances and that their results in no way contradict the view that these mechanisms are located in the blood-forming organs.

Clinical and Experimental Observations upon the Pathology of Trench Frost-bite.—The work upon this subject was stimulated through the numerous cases of frost-bite occurring among the invalided soldiers on the continent. SMITH, RITCHIE and DAWSON (*Jour. Path. and Bacteriol.*, 1915, xx, 159) point out that this has been not uncommon in previous military campaigns, the most notable of which was Napoleon's Russian Invasion. The trench frost-bite has to do entirely with the feet, the exposed hands and face escaping. This is the result of the fact that the feet are tightly enclosed and exposed to semi-frozen mud. Experiments on frost-bite were also undertaken on animals. The essential change in the frost-bite consists in damage of the bloodvessels. After an initial constriction, the exposed vessels show cellular change in their walls which alters their function and permits an excessive amount of fluid to be poured into the surrounding tissue when the cold is removed. The injury is also accompanied by the infiltration of inflammatory cells. The involved areas also suffer the lack of nutrition from vascular constriction with sluggishness of the circulation. The lymphatics of the part are much dilated so that their function is impeded and the tissue fluids are stagnant. Diffuse hemorrhages are also commonly found. They observed that these experimental lesions were very similar to the spontaneous processes in man.

Cardiac Lesions in Goitre.—Disturbance of heart are not alone found in exophthalmic goitre, but also in those of the colloid types. In the latter, it is claimed that the heart suffers mainly from mechanical disturbances of the circulation, rather than as a result of intoxication. To all forms of these cardiac disturbances the term "Kropfherz" is given. There have been relatively few pathological examinations of the heart in goitre, although much data is at hand of clinical studies. Schantz has reported the macroscopic appearance of the heart tissues in cases of colloid goitre, but he has failed to study the tissues histologically. A fatty degeneration of the tissue has been described by several. Bircher studied the hearts of rats in which an experimental goitre had been induced by giving them water from a goitrous district.

The heart muscle, he believes, is directly injured by the harmful agent in the water, this agent, he thinks, attacks the heart and thyroid simultaneously. The majority of authors believe that the injury to the heart is due to a toxic substance liberated by the thyroid. Simmonds examined 8 cases of Baselow, in 7 of which a slight fatty change was found. The histological findings are insufficient to explain the marked clinical symptoms. FAHR (*Centralbl. f. Pathol.*, 1916, xxvii, 1) studied 8 cases of goitre heart, 5 of which were of the Basedow type and 2 of colloid goitre. Two cases of Basedow occurred in girls of twenty-one years. The heart of one was hypertrophied and of the other reduced in size, the muscle tissue of each showed an acute interstitial myocarditis with leukocytic infiltration. The heart muscle showed evidence of degeneration. In two older individuals there was a similar but milder infiltration with fibrosis. Histological changes were found in the muscle tissue of all cases. There was no evidence that the vascular structures of the heart were primarily involved. The author believes that the toxin associated with goitre has a direct effect upon the heart muscle.

Thrombosis of the Mesenteric Arteries.—INGEBRIGSTEN (*Centralbl. f. Path.*, 1915, xxvi, 313) reports 2 cases of thrombosis of the superior mesenteric artery, illustrating the marked difference from embolism of the same vessels. Both of these were observed at autopsy. The thrombosis had developed within leutic vessels. In neither case was there evidence of infarct nor had there been any abdominal symptoms during life. He also reported a third case developing in a patient with mitral endocarditis in which multiple small emboli were followed by thrombosis and infarction of the intestine. Curiously enough, both anemic and hemorrhagic infarcts were present in the bowel.

The Effect of Antiplatelet Serum on Blood Platelets and the Experimental Production of Purpura Hemorrhagica.—For some years attention has been directed to the part played by blood platelets in purpura hemorrhagica. Although none of the studies claim that the abnormal condition of the platelets is the prime factor in this blood dyscrasia, yet it would appear that the influence of various toxic and bacterial agents leads to a sufficient disturbance of these elements that hemorrhagic processes are a common outcome. The work of Duke, Cole and Ledingham has indicated the importance of platelet disturbance under these conditions. LEE and ROBERTSON (*Jour. Med Research*, 1916, xxxiii, 323) obtained an antiplatelet serum by repeatedly injecting a rabbit with guinea-pig platelets. This rabbit serum had both lytic and agglutinative properties which were specific for guinea-pig platelets. They found that the phenomenon of lysis required the presence of complement. In another series of experiments, they found by the inoculation of the antiplatelets serum subcutaneously, intraperitoneally, or intracardiac into guinea-pigs, gave rise to purpura in various grades of intensity. By the intracardiac method, death was produced with relatively small amounts of serum. Hemorrhages occurred in various parts of the body including the intestines. Sometimes the bleeding began within a few hours after the injection. The

platelets in all instances were markedly reduced, falling as low as 16,000. The clotting time of the blood was not altered, although the blood clot showed no contraction on standing. The histological examination of the hemorrhagic areas gave no information as to the manner in which the hemorrhages were produced.

Diabetes Insipidus.—Among the many theories in explanation of diabetes insipidus, attention has been particularly attracted to the nervous system and the glands of internal secretion. The apparent association of cerebral injuries, tumors of the brain, and chronic meningitis with diabetes insipidus has been repeatedly commented upon. More and more, however, the cerebral disturbance has been localized about the hypophysis. Hewlitt, Frank, Simmonds and others were the first to observe the presence of polyuria with disturbances of the pituitary body. Some claimed that the disturbance was due to an oversecretion by the pars intermedia, while others believed that the result was obtained by a diminished function on the part of the pars intermedia, while others believed that the result was obtained by a diminished function on the part of the pars intermedia and the posterior lobe. MEYENBURG (*Ziegler's Beiträge*, 1916, lxi, 550) reported two further cases of diabetes insipidus in which the pituitary body was diseased. The first case was a woman, aged thirty-six years, suffering from symptoms of brain tumor associated with polyuria. At autopsy a tuberculous process was found at the optic chiasm and hypophysis. The posterior lobe was particularly involved. The second case also had manifestations of a cerebral tumor with polyuria and polydipsia. At autopsy a malignant tumor was found surrounding the pituitary. In both cases histological examination showed an almost complete destruction of the middle and posterior part of the hypophyseal gland. The author carried on a series of experiments in which animals were treated by repeated injections of pituitary extract. He was unable to obtain any conclusive results respecting the quantity of urine secreted. The author points out that as many of the endocrinous glands are composed of two or more functionally active tissues it is impossible to separate the pathological process of one from those in the other. It is probable that there is a close interdependence between these tissues of the ductless glands so that the activity of each is closely related to the healthy function of the other. Such interactivity is claimed for the components of the adrenal gland. He then concludes that diabetes insipidus of pituitary origin is not due to a hyper- or hypofunction of the one or other portion of the hypophysis but that a disturbance of any portion is reflected to all portions of this gland. Thus a pathological process situated in any part may disturb the function of the entire hypophysis with diabetes insipidus as one of the manifestations.

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Associate in Surgery, Northwestern University Medical School; Associate Surgeon, Mercy Hospital; Attending Surgeon, Cook County and Provident Hospitals, Chicago.

Octavo, about 900 pages, with 656 engravings. Cloth, $6.00, net.

In the preparation of this work the author has carefully culled from the literature the information which seemed most helpful and with it has combined his own ideas and experience in order to cover the field and to present a clear understanding of this important branch of surgery. Much of the clinical and all of the statistical material has been obtained at the Cook County Hospital, Chicago.

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Clinical Pathologist to University Hospital, Chicago.

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